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# INDIAN MEDICAL ASSOCIATION

VOLUME 30 NUMBER 1 CALCUTTA JANUARY 1, 1958

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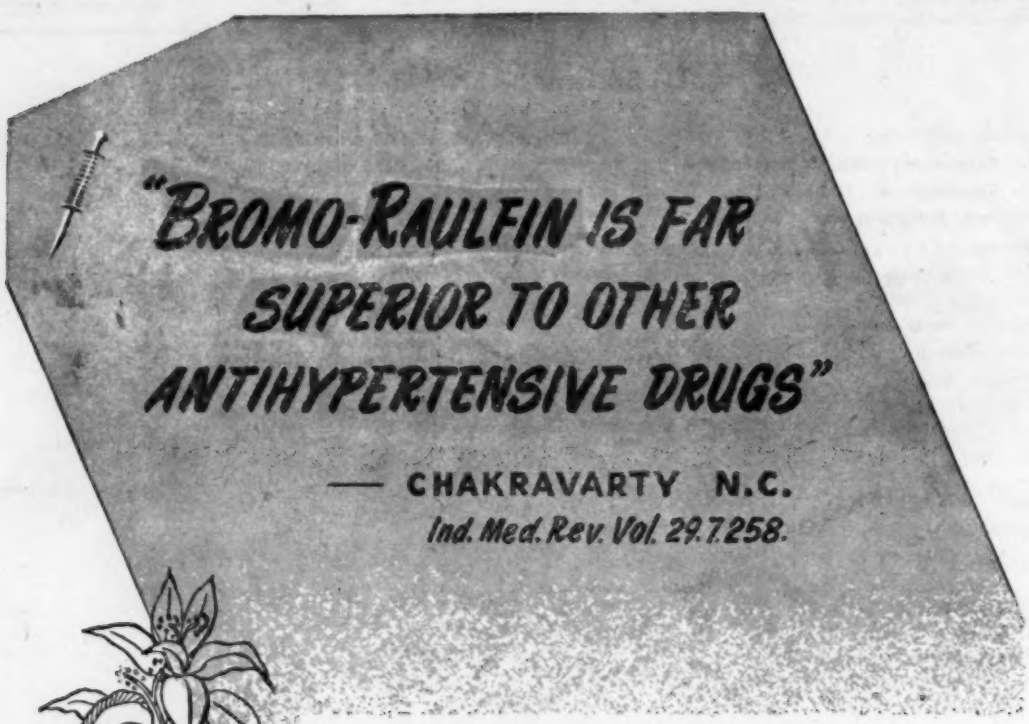


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*Ind. Med. Rev. Vol. 29-7.258*

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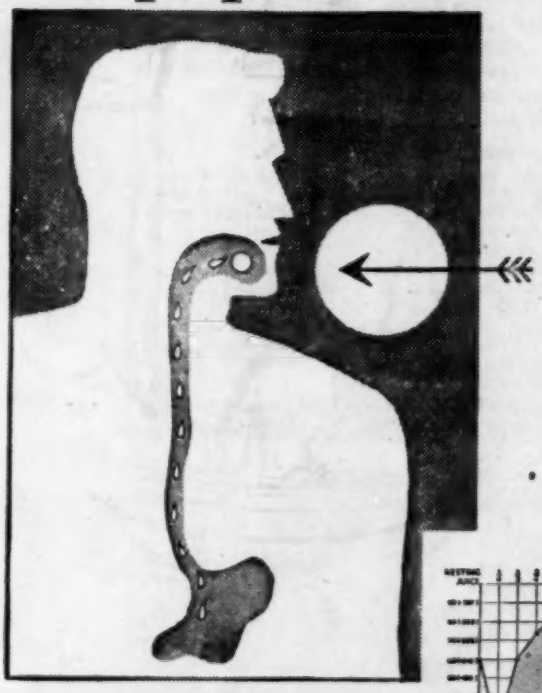

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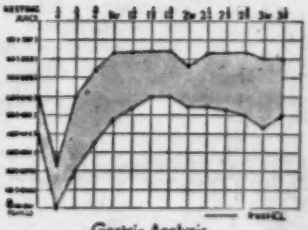
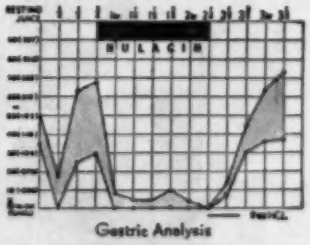


Gastric Analysis

*Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*




Gastric Analysis

*Same patients as in Fig. 1 two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*


### *REFERENCES*

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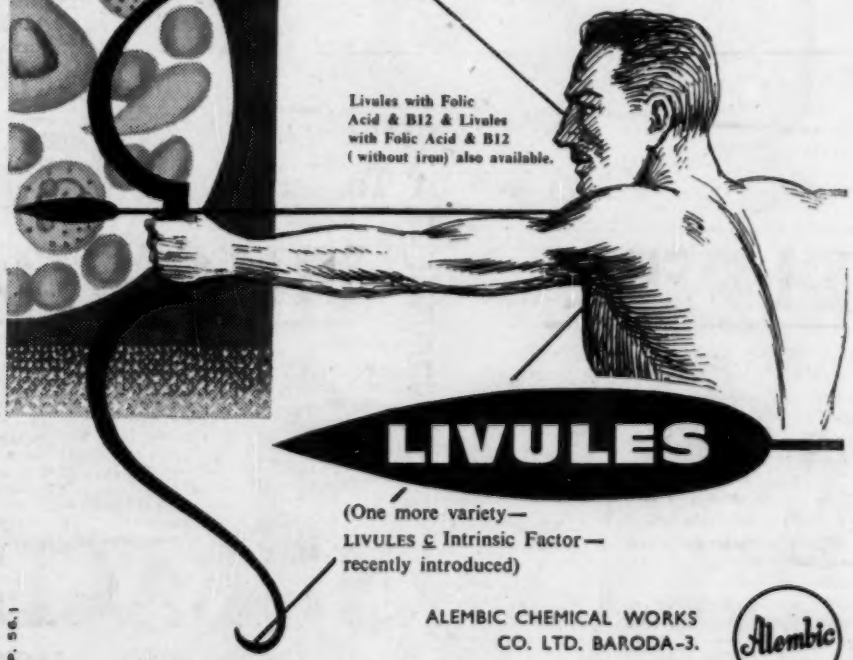

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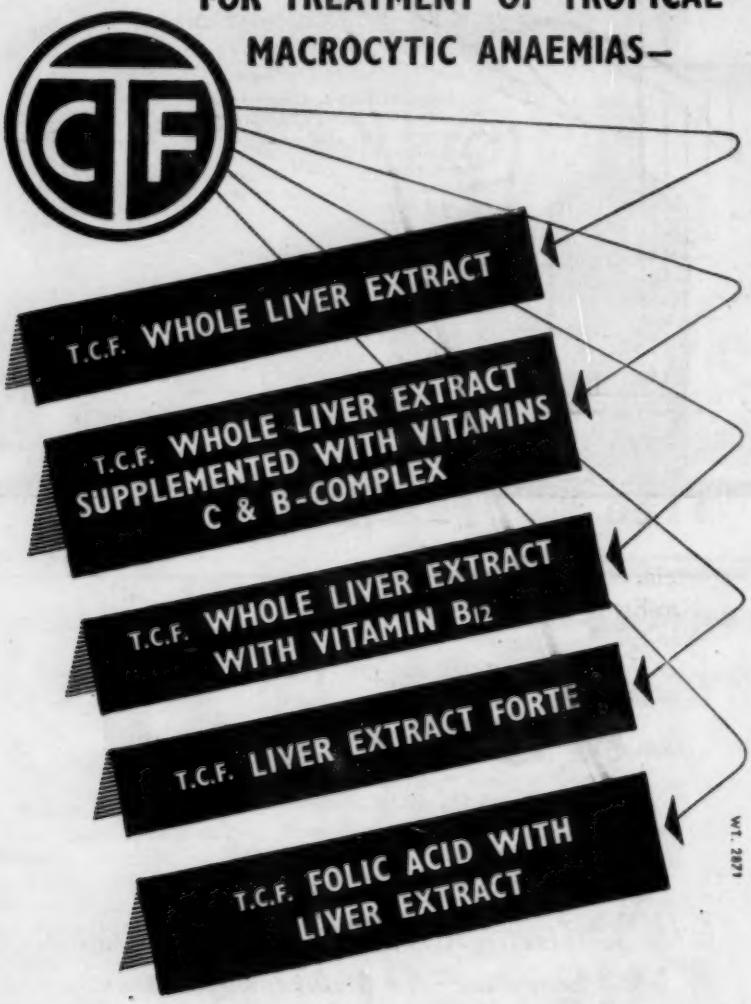
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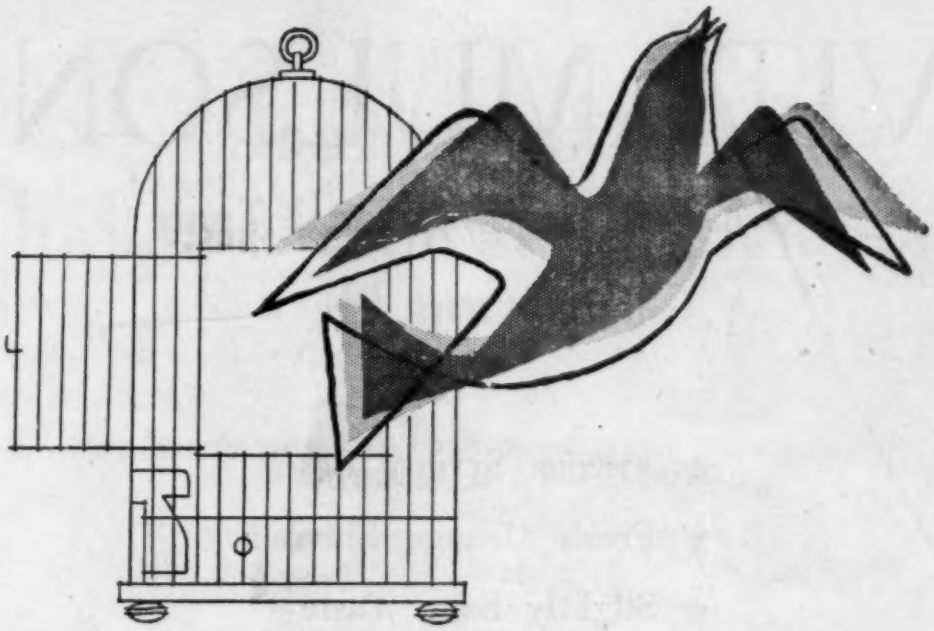

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VOLUME 30 NUMBER 1 — PUBLISHED TWICE A MONTH — EDITOR—P. K. CUHA, M.B., M.R.C.S. (ENG.), D.O.M.S. (LOND.) — CALCUTTA JANUARY 1, 1958

*ORIGINAL ARTICLES*

## EXPERIENCES WITH CHLORPROMAZINE IN THE TREATMENT OF INSTITUTIONALISED PSYCHOTICS

K. BHASKARAN, M.B.B.S., DIP. PSYCH. (MCGILL), CERT. R. C. P. (CAN.)

*Deputy Medical Superintendent, Hospital for Mental Diseases, Ranchi*

AND

L. P. VARMA,* M.D., D.P.M.,

*Medical Superintendent, Hospital for Mental Diseases, Kanke, Ranchi*

The number of articles in scientific journals dealing with clinical trials with chlorpromazine has become legion since its first trial in psychiatric cases by Delay and Deniker (1952). Like all other new introductions in the field of therapeutics, this drug has also gone through an initial phase characterised by over-enthusiasm regarding its range of usefulness and degree of effectiveness, followed by more tempered opinions regarding its place in the treatment of psychiatric disorders. There are certain aspects of the drug-effects about which there seems to be common agreement, viz., its value in more recent cases of psychosis and in cases associated with overactivity, tension or agitation. Opinion is divided, however, regarding its degree of usefulness in the more chronic cases of schizophrenia, the type of cases among the chronic cases it is most beneficial in, the maximum dosage that can be administered with safety and the optimal duration of treatment, etc. While some authors (Vaughan *et al*, 1955) say that it is most effective in catatonic cases which presumably include cases of catatonic stupor, others (Baruk *et al*, 1955) warn against using large dosage of the drug lest catatonogenic action be precipitated. While some authors (Kielholtz and Labhardt, 1956 ; Goldman, 1956) advocate large dosage over a long period of time for best results in chronic cases of schizophrenia, some authors (Kehoe and Pollard, 1956) feel that the effective dose is much lower than most of the published reports indicate. "Those patients who will react favourably do so in a short time and with small dosage." It seems to be increasingly felt that "the indications for therapy are symptomatic and behavioral and not diagnostic." No specific factors seem to be apparent in the group of psychotic patients that can be of use in foretelling the expected response to the drug (Kehoe and Pollard, 1956).

### MATERIAL AND METHOD

The patients for this study were all in-patients of the Hospital for Mental Diseases, Kanke. The various psychiatric syndromes for which the drug was tried are indicated in Table 1. Out of a total number of 110 patients studied, 72 were males and 38 females. The age of the patients ranged from 6 years to 70, the average being 33·6. In all the schizophrenics, excepting the few cases of acute catatonic excitement, insulin coma and/or E.C.T. had been tried without satisfactory results. Out of 63 cases in the groups of chronic catatonic schizophrenia and unclassified schizophrenia shown in Table 1, 19

* Now Superintendent, Indian Mental Hospital, Kanke.

TABLE 1—SHOWING TYPES OF PSYCHOTIC AND THE RESULT OBTAINED AFTER USE OF CHLORPROMAZINE

| Diagnosis | No. of cases | Recovered | Markedly improved | Improved | Unchanged | Worsened |
|---|---|---|---|---|---|---|
| Manic reaction ... ... ... | 6 | 5 | — | 1 | — | — |
| Acute catatonic excitement ... ... | 3 | 2 | 1 | — | — | — |
| Schizo-affective psychosis ... ... | 6 | 3 | 3 | — | — | — |
| Involutional agitated depression ... ... | 5 | 2 | 1 | 1 | 1 | — |
| Paranoid schizophrenia ... ... ... | 19 | — | 3 | 6 | 10 | — |
| Chronic catatonic schizophrenia ... ... | 5 | — | — | — | 4 | 1 |
| Unclassified schizophrenia ... ... | 58 | 1 | 2 | 14 | 41 | — |
| Depression (Manic-depressive psychosis) ... | 1 | — | 1 | — | — | — |
| Postencephalitic behaviour disorder ... | 1 | — | — | 1 | — | — |
| Mental deficiency with behaviour disorder ... | 1 | — | — | 1 | — | — |
| Senile and/or arteriosclerotic psychosis ... | 3 | — | — | 3 | — | — |
| Epilepsy with behaviour disorder ... ... | 2 | — | — | 2 | — | — |
| TOTAL ... | 110 | 13 | 11 | 29 | 56 | 1 |

cases had either transorbital leucotomy or prefrontal leucotomy or both with little or no benefit. These more chronic and refractory cases were specially chosen for the study as, firstly, these patients had had the benefits of other available lines of treatment without appreciable improvement and, secondly, the opinion in published reports regarding the value of the drug in this type of cases was divided and we wanted to come to our own conclusions with respect to the effect of this drug in this type of cases. The average duration of symptoms in these chronic cases (which include chornic catatonic schizophrenia and unclassified schizophrenia of Table 1) was 6·9 years, though it ranged from 3 years to 21 years.

Most of the patients received the medication orally in the form of 25 mg. tablets though intramuscular injection was used in a very few cases where either oral medication was not possible for want of cooperation on the part of the patient or the patient was too excited, aggressive or destructive. To start with, each patient received 25 mg. thrice a day and the dose was gradually increased to a maximum of 300 mg. a day in most cases, though in a few selected cases doses as high as 800 mg. were given. The duration of treatment was 90 days in most cases though in some selected cases the drug was given for as long as 180 days. The shortest period the drug was given for any patient was 21 days.

During the administration of the drug, any side effects and complications that might occur were looked for. Pulse rate was checked 4 times a day, blood pressure twice a week, total and differential W.B.C. count and E.S.R. once a week and urine examined with particular reference to the presence of bile salts and pigments once a week. The patients were interviewed by one of the authors once in 10 days or two weeks to assess the clinical progress. In the final assessment of the results, 5 categories of response to the drug were recognised, viz., "recovered", "markedly improved", "improved", "not changed" and "worsened". A patient was said to have "recovered" when he was totally free from all symptoms, productively employed himself in the occupational therapy department, socialised adequately with other patients and the staff and had gained some insight into his mental condition. He was said to have "markedly improved" when he was totally or almost totally free from symptoms but his productivity in the occupational therapy department and/or his socialisation was not yet adequate for consideration for discharge. He was said to be "improved" when there was an appreciable amelioration of symptoms but still he had them to a disabling extent and his productivity in the occupational therapy department and socialising abilities were still far from adequate. The categories of "not changed" and "worsened" are self-explanatory. The final assessment of the response to the drug was arrived at in every case by one or other of the authors with the help of the reports on the patient by the occupational therapist, ward sisters, social worker and physical instructor and a detailed psychiatric interview.

## RESULTS

Results are indicated in Table 1. As can be seen from the table the cases that showed the most satisfactory clinical response to the drug were cases of manic reaction, acute catatonic

excitement, schizo-affective psychosis, involutional agitated depression and paranoid schizophrenia in that order. Out of five chronic catatonic schizophrenics, none improved and one actually showed worsening of the symptoms. Of the 58 cases of unclassified schizophrenia, 41, i.e., 70 per cent showed no appreciable improvement with the drug, only 17 (30 per cent) showing improvement. The cases that fell into the group of "recovered" and "markedly improved" in this group were only 3 out of 58 (scarcely little over 5 per cent). It should be stated in this connection however that in most of the patients on the drug some degree of beneficial effect was noticed in the form of improved appetite with more or less weight gain, sedation without sleepiness, and more cooperative behaviour. Many other authors would have probably referred to these cases as having "slightly improved" or "mildly improved", but we felt it desirable to leave out this "category" as it would tend, inevitably to make the categorisation confusingly wide and arbitrary. This will probably account for our relatively large percentage of cases of unclassified schizophrenics being marked as "unchanged" in the assessment of their response to the drug. Another factor to be borne in mind in this connection is that most of these patients were very chronic with an average duration of illness of 7 years and with a decidedly poor prognosis as indicated by the fact that in most of them the various physical methods of treatment including leucotomy had been unsuccessful. In the group of paranoid schizophrenics, that showed very satisfactory clinical response to the drug, a feature that was noticed as compared with the group that did not show the same degree of improvement was that these former patients had not totally severed their ties with reality. They were still making an attempt to establish some kind of relationship with the world of reality though with a considerable amount of stress. For example, one of the paranoid patients, who was grouped in the markedly improved category, had the delusion that people were inserting their penises into his mouth when he was asleep. He sought to get relief from these persecutors by persistently complaining about them to the physician and frequently picking quarrels with other patients, whom he suspected to be the persecuting agents. Two features that were found to be present in the majority of cases in the "unchanged" group were marked apathy or thinking disorder.

Seven cases which showed some appreciable degree of improvement with the treatment manifested signs of relapse, 3 of them while being on a maintenance dose and the rest, 2 to 4 months after discharge from the Hospital. Of these seven cases, 2 were cases of manic reaction, 3 of schizo-affective psychosis and 2 of unclassified schizophrenia.

Table 2 indicates the undesirable side-effects and complications attending the use of this drug and the relative frequency of their incidence. It was possible to readminister the drug after a temporary stoppage in the case of most side-effects though readministration was not attempted in cases associated with complications like jaundice, agranulocytosis and epileptiform fits.

TABLE 2—SHOWING THE SIDE REACTIONS NOTED AFTER THE USE OF CHLORPROMAZINE

| Side-effects and complications | No. of cases | Percentage incidence |
|---|---|---|
| Transitory tachycardia ... | 16 | 15 |
| Transitory irregularity of pulse ... | 8 | 7 |
| Transitory hyperpyrexia ... | 8 | 7 |
| Transitory parkinsonian syndrome | 24 | 22 |
| Maculopapular rash ... ... | 4 | 4 |
| Transitory gastrointestinal disturbances ... ... ... | 5 | 5 |
| Jaundice ... ... ... | 1 | — |
| Agranulocytosis ... ... | 1 | — |
| Neutropenia (not showing clinical features of agranulocytosis) ... | 4 | 4 |
| Epileptiform fits ... ... | 1 | — |

## DISCUSSION

Our findings agree with those of the majority of authors about the value of chlorpromazine in the treatment of manic reactions, catatonic excitements and schizo-affective psychosis. It was also of value in involutional agitated depression and some selected cases of paranoid schizophrenia. The drug was of little use in cases of chronic schizophrenia characterised by apathy or thinking disorder or paranoid ideation with little or no attempt to re-establish relationship with the world of reality. Our findings substantiate those of Kehoe and Pollard (1956) that increasing the dose of the drug or the duration of treatment beyond an optimal level (in our experience 300 mg. a day or 90 days respectively) was not attended with any more favourable therapeutic results.

There is as yet no agreed view about the mode of action of chlorpromazine. There is increasing evidence on the basis of experimental investigation with the drug in animals that it "depresses the spontaneous activity of the reticular formation of the brain stem and diminishes their sensitivity

to afferent sensorial or nociceptic impulses" (Courvoisier, 1956). It was shown in condition-reflex experiments with rats using auditory stimuli that chlorpromazine in low dosage definitely retards the response to the auditory stimulus as well as slows down the speed. In an increased dosage there is an inhibition of the response. In general, the rats treated with chlorpromazine becomes disinterested in the bell ringing which no longer incites flight from pain (Courvoisier, 1956). It is of course difficult to apply these findings in animals to human situations. One can hypothesise, however, on the basis of these findings that the drug possibly diminishes the response in the patients to the various sensory cues including the symbolic and the social ones. The fact that the maximum clinical response to the drug is shown by those patients whose contact with the world of reality and social stimuli is preserved to a greater or lesser extent as compared with cases who have altogether severed their relationship with the social world indicates that these animal studies might have some relevance to experiences with the drug in human population. A manic who is very much alive and sensitive to external environment and an excited catatonic who strives to effect a restitutional process, though in a psychotic way, are benefited far more than a stuporous schizophrenic who is totally withdrawn from the world of reality and is oblivious to all kinds of social stimuli from outside world, and makes no efforts at restitution. In this connection, the observations of Petries (1956) are interesting and relevant. They found on comparison between chlorpromazine treated patients and lobotomised patients that those on chlorpromazine showed increased score on introversion variables while lobotomised patients showed marked decrease. This may possibly explain the lack of beneficial response of the drug on already withdrawn introverted group of patients and occasional worsening of stupor symptoms in catatonic stupor cases. The drug probably has also a non-specific action on the processes, that determine the self-maintaining cycle of mental activity which maintains the agitation and overactivity in some other psychoses like involutional agitated depression and psychoses associated with mental deficiency, encephalitis, etc., in which cases also it has beneficial effect.


### Summary

Experiences with the use of chlorpromazine in 110 hospitalised psychotics are described. The type of cases, the benefit obtained by the drug and the side-effects attending its use are also described. The mode of action of the drug is briefly discussed.



### Acknowledgment

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## Hb.S-THALASSAEMIA DISEASE IN INDIA


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Sickle cell anaemia and sickle cell trait represent respectively homozygous and heterozygous forms of an abnormal haemoglobin known as haemoglobin (Hb.) S. 'Sickling' since its first demonstration in an American Negro in 1910 by Herrick, was, for a long time, regarded as an exclusive 'Negro' character. Subsequent studies have shown the presence of Hb.S in non-negro population as well, viz., in Greeks (Cooley and Lee, 1929 ; Choremis *et al*, 1953 ; Choremis and Zannos, 1957) in white Americans (Clarke, 1934), in Italians (Wiener, 1937), in Yemenite Jews (Dreyfuss and Benyesch, 1951), in Arabians (Lehmann, 1954), Algerian Muslims (Portier *et al*, 1954), and Eti-Turks (Aksoy, 1955). In India it has been been reported from South India (Lehmann and Cutbush, 1952), Oriya and Bihari immigrants in Assam (Dunlop and Mozumder,

1952), Uttar Pradesh (Bhatia *et al*, 1955), Mahar and Kunbis of Madhya Pradesh (Shukla and Parande, 1956 ; Shukla, 1957) and Western India (Buchi, 1955 ; Sukumaran *et al*, 1956, Lehmann and Sukumaran, 1956 ; Nail *et al*, 1957).

Thalassaemia for which no abnormal haemoglobin has so far been implicated, but which nevertheless represents a hereditary defect in haemoglobin synthesis, appears to be present almost all over India. The genes responsible for thalassaemia and Hb.S are different and are located on different chromosomes and are non-allelomorphic. Thus in a country where both thalassaemia and Hb.S are prevalent, it is possible that a single individual may possess these two non-allelomorphic genes, giving rise to a condition now known as Hb.S-thalassaemia disease. The first instance of such a condition was recorded in an Italian family by Silvestroni and Bianco in 1945 under the caption microdrepanocytic anaemia. Many similar cases have since been described from Greece, Italy, Turkey, South America and United States (Zuelzer *et al*, 1956 ; Choremis and Zannos, 1957).

No authentic case of Hb.S-thalassaemia has so far been reported from India. The case described recently by Nail *et al* (1957) is only presumptive as discussed by the authors themselves.*

In view of scanty information so far available regarding the haemoglobinopathies in India, it was thought worthwhile to report in detail the first instance of Hb.S-thalassaemia disease encountered during critical analysis of a series of patients suffering from hereditary haemoglobinopathy (Annual report of the Haematological Unit, I.C.M.R. 1956-57).

## Material and Methods

In Calcutta, we have since 1946, come across 200 patients of hereditary haemoglobinopathies which until recently were considered to be instances of homozygous thalassaemia. Characterisation studies have recently shown that this group consists mostly of Hb.E-thalassaemia (Chatterjea *et al*, 1956, 1957a). Comprehensive investigations including confirmatory family studies have so far been completed in 92 patients which consists of Hb. E-thalassaemia 80, homozygous thalassaemia 11, and Hb.S-thalassaemia 1. The present communication is an account of our observations on the single instance of Hb.S-thalassaemia disease in this series.

In addition to routine clinical and haematological studies, the following investigations were done on the patient, her parents and two siblings.

(i) Sickling test with 2 per cent solution of sodium metabisulphite (Daland and Castle, 1948).

(ii) Foetal haemoglobin by the alkali denaturation technique (Singer *et al*, 1951).

(iii) Plasma haemoglobin by the method of Bing and Baker (1931).

(iv) Electrophoretic analysis of haemolysate with a LKB paper electrophoresis equipment using veronal buffer at pH 8·6 and ionic strength 0·05. The runs were usually conducted for 8 hours with a constant current of 0·5 milliampere per cm. applied at a voltage of 200-250 D.C. Samples showing two distinct spots were compared with known samples of abnormal haemoglobins. Quantitation of electrophoretograms was made in a Photovolt Densitometer.

### Clinical Data

A. D., a ten-year-old girl attended the Haematology Out-patients' Clinic on 5-8-57 with a history of low grade fever and hepatosplenomegaly of 2 years' duration. She also complained of occasional epistaxis for the last one year. On examination, the patient looked slightly pale and appeared to be undersized. She weighed 36 lb. Conjunctivae were icteric and a few cervical lymph nodes were enlarged and palpable with no evidence of tenderness or matting. The spleen was enlarged (7·5 cm. below the left costal arch) and firm in consistency. The liver was also enlarged (2·5 cm. below the right costal arch), smooth and firm. Cardiovascular, respiratory and other systems did not reveal any significant abnormality.

### Laboratory Data

The details of haematological, biochemical and electrophoretic data are given in Table 1 and Fig. 1 (*vide* Plate). The patient showed moderate anaemia with marked anisocytosis, poikilocytosis and hypochromia in peripheral blood smear. There were a few sickle cells in the Leishman stained peripheral blood smear and sickling test was strongly positive (Fig. 2, *vide* Plate). Plasma bilirubin measured 1·0 mg. and plasma haemoglobin 15 mg per cent. Hb.S approximated 83 per cent with Hb. F constituting 17 per cent. Hb.A was virtually absent.

Coomba' test was negative. There was no demonstrable anti-red cell antibody in the serum. W.R. was negative. Aldehyde test and complement fixation test for kala-azar were negative. Radiological examination of the skull and the long bones of the forearms showed the evidence of slight osteoporosis. Total serum vitamin $B_{12}$ level was 400 micromicrogram per ml. (normal value 90-600). Twenty-four hours' excretion of folic acid following a 5 mg. subcutaneous injection of folic acid was 3·92 mg. (normal value should not be below 1 mg.).

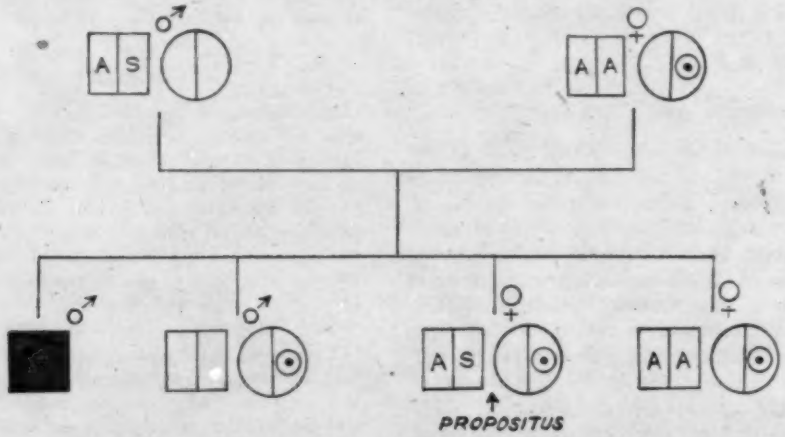
* Since the completion of this manuscript personal communication from Shukla and from Sukumaran indicates that they have recently come across cases of Hb. S.-thalassaemia.

FAMILY DATA

Photograph of the patient with her father, brother and sister is given in Fig. 3. Family tree is shown in Fig. 4 and relevant laboratory data shown in Table 1.

*Mother*, 35-year-old Bengalee Hindu woman, born of Bengalee parents who had been residing in Bengal for generations. She did not have any presenting complaint but on direct interrogation she gave history of chronic ill-health which from time to time had been ascribed to anaemia. On physical examination, apart from slight pallor, she did not present any other abnormality. Blood examination showed slight anaemia with marked abnormality of red cell morphology, suggesting thalassaemia trait. Sickling test was negative. Hb.F measured 3·3 per cent. Electrophoretogram revealed a single spot in the

FIG. 3—PHOTOGRAPH OF THE PATIENT (2ND FROM LEFT) SHOWING HEPATOSPLENOMEGALY WITH HER FATHER, BROTHER AND SISTER.




Symbols— A A NORMAL. A A - THALASSAEMIA HETEROZYGOTE.

A S - Hb-S. HETEROZYGOTE. A S - Hb-S. THALASSAEMIA

—DIED IN INFANCY.

FIG. 4—FAMILY TREE OF THE PATIENT (A.D.)

TABLE 1—RELEVANT CLINICAL AND HAEMATOLOGICAL DATA OF A.D. (HB. S-THALASSAEMIA) AND FAMILY

| | Patient A.D. | Father M.D. | Mother S.D. | Sister S.D. | Brother A.D. |
|---|---|---|---|---|---|
| Age (years) ... | 10 | 64 | 35 | 8 | 11 |
| *Clinical features* : | | | | | |
| Symptoms ... ... ... | + | Nil | Nil | Nil | Nil |
| Spleen ... ... ... | 7·5 cm. | 0 | 0 | 0 | 0 |
| Jaundice ... ... ... | Slight | 0 | 0 | 0 | 0 |
| *Haematological* : | | | | | |
| Hb. g. (%) ... ... ... | 8·7 | 13·3 | 8·7 | 12·2 | 11·6 |
| R.B.C. m/c.mm. ... ... ... | 3·2 | 5·2 | 3·5 | 3·9 | 4·2 |
| Ret. (%) ... ... ... | 8·5 | 0·2 | 3·0 | 1·0 | 0·5 |
| P.C.V. % ... ... ... | 26·0 | 43·0 | 29·0 | 37·0 | 38·0 |
| M.C.V. (cu.$\mu$) ... ... ... | 82·0 | 82·0 | 90·0 | 94·0 | 88·0 |
| MCH ($\gamma\gamma$) ... ... ... | 27·0 | 25·0 | 24·0 | 31·0 | 27·0 |
| MCHC (%) ... ... ... | 34·0 | 30·0 | 30·0 | 33·0 | 30·0 |
| *Red cell morphology* : | | | | | |
| Anisocytosis ... ... ... | ++ | 0 | + | 0 | 0 |
| Poikilocytosis ... ... ... | ++ | 0 | + | 0 | 0 |
| Hypochromia ... ... ... | ++ | + | + | 0 | + |
| Target cells ... ... ... | ++ | 0 | + | + | 0 |
| Oval cells ... ... ... | 0 | 0 | + | + | 0 |
| Polychromasia ... ... ... | + | 0 | 0 | 0 | 0 |
| Stippled cells ... ... ... | 0 | 0 | 0 | 0 | 0 |
| Spherocytes ... ... ... | 0 | 0 | Occasional | Occasional | 0 |
| Sickle cells ... ... ... | + | 0 | 0 | 0 | 0 |
| Premature cells in peripheral blood ... | 0 | 0 | 0 | 0 | 0 |
| Osmotic fragility ... ... ... | 0·4—0·18 | 0·48—0·2 | 0·4—0·24 | 0·4—0·20 | 0·44—0·20 |
| Total plasma bilirubin (mg. %) ... | 1·0 | 0·2 | 0·2 | 0·2 | 0·2 |
| Foetal Hb. % ... ... ... | 17 | 1·19 | 3·26 | 1·63 | 1·04 |
| Plasma Hb. mg. % ... ... ... | 15 mg. | – | – | 3·7 | 1·9 |
| Sickling test ... ... ... | +ve | +ve | –ve | –ve | –ve |
| Electrophoretic pattern ... ... | S F/A | AS | AA* | AA* | AA* |
| Diagnosis ... ... | Hb. S-thalassaemia | Hb. S trait | Thalassaemia trait | Thalassaemia trait | Thalassaemia trait |

* Raised level of $A_2$ was demonstrable in 3 MM paper

A position. A course of ferrous sulphate did not improve her blood picture.

*Father*, aged 64, had no complaints even on direct interrogation. He was born in Ranchi—a district in Bihar. His grandfather embraced christianity. His parents were Rajput christians who had been living in Bihar for at least three generations. Whereabouts of earlier ancestors were not traceable. In his family there was no history of intermarriage with aboriginal tribes. Physical examination was essentially normal. Haematological examination was also normal except for slight hypochromicity and osmotic resistance of the peripheral red cells. Sickling test was strongly positive and electrophoresis showed an AS pattern.

First brother died in infancy. Living siblings—*brother* aged 11 and *sister* aged 8 did not have any presenting complaint. They had slight anaemia and their other haematological data, though less conspicuous than their mother's, were compatible with the diagnosis of thalassaemia trait.

## DISCUSSION

In India the incidence of Hb.S in the general population must be very rare. In random examination of at least 10,000 blood samples mostly from Bengalees tested with sodium metabisulphite, supplemented with electrophoretic analysis in 1000 cases, we have not, so far, found a single instance of S haemoglobin except in the family referred to above. In this case of Hb. S-thalassaemia disease, Hb.S was inherited from Rajput father and thalassaemia from Bengalee mother. Most of the instances of Hb.S have so far been recorded in aboriginal tribes. Thalassaemia on the other hand is commoner in the general population. In a series of 700 unrelated Bengalee Hindus, a 3·7 per cent incidence of thalassaemia was recorded (Chatterjea *et al*, 1957b).

Hb. S-thalassaemia represents an heterozygous

condition for Hb. S, yet the percentage of haemoglobin S is more than 80 which is considerably higher than expected. It appears that interaction of thalassaemia is responsible for the enhanced expressivity of Hb. S (and also of F) and suppression of Hb. A. Such disproportionately high percentage of abnormal haemoglobin appears to be a regular feature not only in Hb. S-thalassaemia (Humble *et al*, 1954 ; Zuelzer *et al*, 1956 ; Singer *et al*, 1957), but also in Hb.E-thalassaemia (Chatterjea *et al*, 1957), both of which represent instances of interaction of thalassaemia gene with genes for abnormal haemoglobins.

The present study incidentally shows the value of family studies in the differential diagnosis between sickle cell anaemia and Hb. S-thalassaemia. In this particular instance if the mother was not available for examination, from the other available data, it would not have been possible to exclude sickle cell anaemia.


### Summary

An instance of Hb. S-thalassaemia is described in a ten year old Indian girl. The girl presented haemolytic anaemia of moderate degree. Different findings suggest interaction between genes for thalassaemia and Hb.S.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## SICKLE CELL ANAEMIA IN ASSAM


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### Introduction

Since Herrick (1910) first described sickle cell anaemia in an American Negro many cases have been reported, mostly amongst members of the Negro race, with occasional cases occurring amongst Caucasian Greeks, South Italians and Mexicans.

More recently Lehmann (1952) detected the occurrence of the sickle cell trait in India amongst the aboriginal communities of the South.

Dunlop and Mozumder (1952) drew attention to the prevalence of the sickle cell trait amongst the immigrant labour population of Orissa working on tea plantations in Upper Assam. They described several cases of haemolytic anaemia associated with sickling which they diagnosed as sickle cell anaemia. Since then, we have been unable to find any further case reports in the literature. Nevertheless, since sickling has been found in this population, a proportion presumably

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will be homozygous for the haemoglobin S gene, or else heterozygous but combined with another abnormal haemoglobin, and thus liable to suffer from haemolytic anaemia (Neel, 1949).

It is not surprising, therefore, that we have recently come across three cases of sickle cell anaemia in this medical practice. Since the published reports of the disease from this part of the world are scarce, we think it worth while giving a short record of these cases.

### Case Reports

Case 1—S. N., a male child, aged 4½ years, born in Assam of immigrant parents from Orissa, came under the care of the authors at Beesakopie Central Hospital on 23-8-1956.

*Past history*—The child is stated to have been suffering from periodic "low fever" and anaemia with remissions and intermissions since he was six months old. The liver and the spleen were not palpable on first admission but were found to be palpable a few months later and gradually increased in size. Blood smears for malaria parasites proved to be negative on repeated examination. For a period of three months there was pain and swelling of the big joints of the extremities and finger joints, accompanied by discrete enlargement of cervical glands. The condition was variously treated with salicylates, cortisone, and aureomycin, followed by streptomycin for a few weeks, and appears ultimately to have subsided. The anaemia apparently improved with anti-anaemic therapy (ferrous sulphate and folic acid), only to relapse after an interval of a few months.

*Family history*—The parents and all the siblings except the one described in Case 2 were in good health.

*On examination*—The child was pale and emaciated and the growth was stunted for the age. There was no obvious deformity of the skull or long bones and no signs of leg ulceration. The temperature varied from 99°—100°F. The liver and spleen were enlarged to 2 fingers' breadth below the costal margin on each side of the abdomen and were hard to the touch. No other abnormality was found on clinical examination apart from a soft precordial systolic murmur.

*Laboratory investigations* (Table 1)—The blood was repeatedly negative for malaria. There was a macrocytic normochromic anaemia with many normoblasts in the peripheral blood smear and a constant reticulocytosis; the serum bilirubin was raised and the urinary urobilinogen increased. All these findings pointed to a haemolytic origin of the anaemia. A fragility test was carried out, with the possibility of congenital haemolytic jaundice in mind. Somewhat to the authors' surprise the fragility was markedly decreased, complete lysis of the red cells not occurring even in distilled water. A sealed preparation of blood was then made and this showed marked sickling of the red cells in less than one hour. The Coombs' test for blocking antibodies was negative, thus making unlikely a diagnosis of haemolysis due to circulating haemoagglutinins or haemolysins.

The skiagram of the skull showed marked thickening of the frontal bones. Such thickening of the calvarium is a feature of some cases of sickle cell anaemia (Wintrobe, 1951).

In view of the decreased fragility, sickling of the red cells and skull changes, together with the features of a haemolytic anaemia, a provisional diagnosis of sickle cell anaemia was made.

Case 2—K. N., an infant of one year, and the brother of Case 1, was admitted to Beesakopie Central Hospital in April 1957 with painful swellings of the arms and legs for the past four months. The right elbow region and the metacarpophalangeal joints were found to be tender and swollen. Following admission the swelling of the ankle joints occurred. The child was found to be anaemic (Table 1) and to have evidence of blood regeneration in the form of circulating normoblasts and a reticulocytosis. On account of his relationship to Case 1 he was tested for sickling, and this was positive, but fragility was only slightly diminished, and red cell destruction did not appear to be increased, as indicated by the urinary urobilinogen level. There were radiological changes in the neighbourhood of the right elbow joint.

The multiple joint swellings were at first considered probably to be unrelated to the anaemia. The radiological changes and subsequent follow-up study, however, made it clear that the arthritic manifestations were quite consistent with those seen in sickle cell anaemia.

The parents and other children were then investigated for the sickle cell trait. The findings are shown in the family tree (Fig. 1) and from these we made the tentative

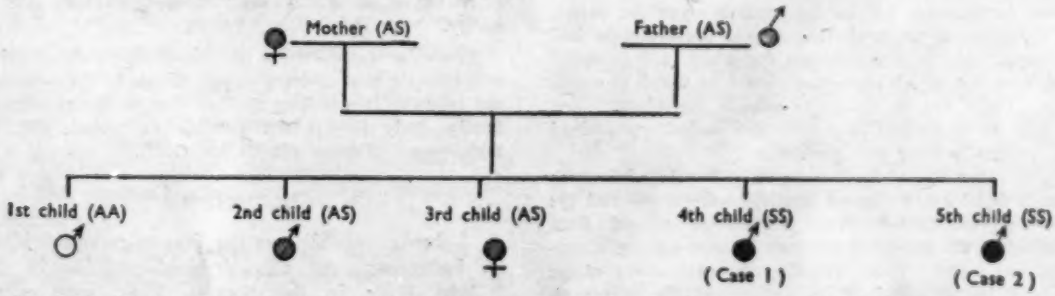
Mother (AS)
Father (AS)
1st child (AA)
2nd child (AS)
3rd child (AS)
4th child (SS)
(Case 1)
5th child (SS)
(Case 2)
A = Adult Hb S = Sickle cell Hb 0 = No sickling (AA) = Sickle cell trait (AS) = Sickle cell homozygous (SS)

Fig. 1—Family Tree in Cases 1 and 2.

TABLE 1—SHOWING LABORATORY FINDINGS

| Name | S. N. | K. | J. B. |
|---|---|---|---|
| R.B.C. in million per c.mm. ... | 1·3 | 2 | 2·3 |
| Hb. g. % ... ... ... | 4·5 | 6 | 8 |
| MCHC (%) ... ... ... | 30 | 27·8 | 34 |
| P. C. V. (%) ... ... ... | 15 | 22 | 23 |
| M. C. V. (cu.$\mu$) ... ... | 115·3 | 110 | 100 |
| W. B. C. per c.mm. ... ... | 12,980 | 16,460 | 9,200 |
| Normoblast C ... ... ... | ++ | ++ | |
| Reticulocyte (%) ... ... | 37·1 | 16·9 | 27·3 |
| M.P. ... ... ... | Not seen | Not seen | Not seen |
| Red cell fragility ... ... | Begins at 0·36% NaCl but lysis not complete even in distilled water | Begins at 0·44% NaCl and complete at 0·28% NaCl | Begins at 0·48% NaCl but lysis not complete even in distilled water |
| Sickling test ... ... ... | ++++ in one hour | ++++ in four hours | +++ in one hour |
| Paper electrophoresis of haemoglobin | SS | SS | |
| Foetal Hb % ... ... ... | 9·53 | 20·1 | |
| Serum bilirubin ... ... | 2·2 mg. per 100 ml. | | 7·5 mg. per 100 ml. |
| Coombs' test ... ... ... | Negative | Negative | Negative |
| Kahn test ... ... ... | Negative | | Negative |
| URINE : | | | |
| Urobilinogen ... ... | ++ in 1 :15 dil. | Trace in 1 :10 dil. | ++ in 1 :15 dil. |
| Bilirubin (Fouchet test) ... | Negative | Negative | Weak positive |

assumption that both parents were probably heterozygous for haemoglobin S and that the affected children with sickle cell anaemia were homozygous. That this was in fact the case was shown by the kindness of Dr. J. B. Chatterjea, Professor of Haematology, Calcutta School of Tropical Medicine, who carried out haemoglobin electrophoretic studies on the patients and their parents and siblings. His results are shown in the table and on the family tree (Table 1 and Fig. 1).

CASE 3—J. B., male, aged 20 years, born in Orissa, migrated to an Upper Assam Tea Plantation when a child with his parents. He was transferred from one of the garden hospitals in the practice to Beesakopie Central Hospital on 21-6-1956.

*Family history*—Patient is the only child of the parents who died some years ago, and no other history was available.

*Past history*—The patient had been treated several times for anaemia but no information as to the nature of the anaemia was available. A year previously he had an acute pain in the abdomen for which a laparotomy was done but no adequate cause could be found at operation. There was no history of pain in the joints.

*History of present condition*—The patient complained of low grade fever and weakness.

*On examination*—An emaciated and pale adult with scanty facial hair : The conjunctivae were icteric and the chest pigeon-breasted. The temperature ranged from 98·5°—99·5°F. No bony abnormality and no leg ulceration was found. There was discrete enlargement of the cervical lymph glands. The spleen and the liver were both three fingers' breadth enlarged. Heart : The apex beat was found in the 5th interspace 4" from the midsternal line and a systolic bruit was heard over the mitral area; B.P. was 108/48 mm. Hg.

Laboratory investigation (*vide* Table 1) during his 4 months' stay in hospital showed :

(1) An anaemia which was microcytic on admission, changing to slight macrocytosis. Ferrous sulphate was the only drug given during the period.

(2) Constant reticulocytosis noted on repeated examinations, together with increased urinary urobilinogen and a raised serum bilirubin level.

(3) Decreased fragility of red cells, complete lysis not taking place even in distilled water.

(4) A sealed cover slip preparation showed marked sickling of the red corpuscles after one hour.

(5) Coombs' test negative.

(6) Blood sugar repeatedly negative for malaria parasites.

(7) Skiagram of the skull showed no bony abnormality.

From the above data, a provisional diagnosis of sickle cell anaemia was made, although clinically the case was not typical. It was later realised that in the absence of family study it was not possible to exclude Hb. S-thalassaemia disease (Chatterjea, 1957).

## DISCUSSION

Lehmann (1952) was the first to report sickling in India amongst the Veddoid peoples in the Nilgiri Hills in the South. Very soon after, Dunlop and Mozumder observed sickle cell anaemia in Upper Assam amongst the Oriah immigrant

labourers from Orissa State in East Central India. It is uncertain to which great racial group these people belong, though they are considered as "aboriginal".

Other cases have been recorded, from the Marhar community of Madhya Pradesh (Shukla and Parande, 1956); and Foy *et al* (1956) have noted sickling, varying widely, from 3 per cent to 55 per cent, within subsections of the same tribe, amongst the Kondhs. So far, in this district, we have only come across sickling in the Oriahs, but other racial groups have not yet been seriously examined. A pilot investigation of the local Assamese people, who in general do not work in the tea gradens, is in progress.

In a sample survey carried out on Oriahs in this medical practice we have found a sickle cell trait incidence of 15 in 100 people examined. On a neighbouring tea estate practice Dunlop (1957) has found an incidence of 29 in a random sample of 100 Griza Oriahs.

Neel, as quoted by Allison (1956), has estimated that if trait carriers are heterozygous and anaemia patients homozygous for the sickle cell gene, the expected ratio would be 39:1. In practice, in African populations where the trait occurs in the neighbourhood of 20 per cent, sickle cell anaemia has been found in about 1 per cent of infants. Thus it may be that about 1 per cent of the infant Oriah children are in fact suffering from sickle cell anaemia.

It is interesting that, apart from Dunlop and Mozumder's (1952) patients, apparently no other cases of sickle cell anaemia have been reported from Assam, despite the fact that the trait is common. The explanation probably lies in the fact that the recognition of sickling in Assam is of recent origin and that, before this, sickle cell anaemia was not seriously considered in the differential diagnosis of the anaemias. Further, other causes for the very prevalent anaemias were usually not far to seek. It may also be that there are few survivors into adult life; case taking and investigation of the infant patient presents greater difficulty than in the adult, so that infant patients may tend to remain incompletely diagnosed.


### Summary

Two cases of sickle cell anaemia are presented and the reasons for arriving at this diagnosis are discussed.

In Cases 1 and 2 the family history is suggestive of heterozygous parentage for the haemoglobin S gene, and this is borne out by haemoglobin electrophoresis studies.

In a pilot survey, the incidence of sickling amongst immigrant workers from Orissa in South-East India was found to be 15 per cent.

The reasons for the comparative rarity of reported cases of sickle cell anaemia in Assam are discussed.



### Acknowledgment

It is a pleasure to record our indebtedness to Dr. J. B. Chatterjea for the electrophoretic studies, and to the Assistant Medical Officers of Baghjan and Samdang T. E. Hospitals for referring the patients.


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## COLOUR BLINDNESS WITH SEX-LINKED HEREDITY*


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The colour sense is the faculty whereby we are able to distinguish different colours and different colour tones. Normal colour vision is a function of our consciousness. It might seem strange that a particular coloured light of a particular wave length will not produce the same sensation of colour with everybody. It appears that there are large individual differences amongst mammals but, on the whole, dogs can appreciate differences

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of hue as well as brightness. Colour discrimination is a function of cerebral cortex and it disappears in decorticated animals while reactions to change of luminosity still persist.

According to Parsons (1915), attention was first drawn to the colour vision of primitive people by Gladstone (1858). In his "Studies on Homer and the Homeric Age" he drew attention to the vagueness of the colour terminology of Homer and concluded that the ideas of colour at that time must have been different from our own. Geiger (1868), quoted by Parsons (1915) remarked that colour sense of the ancient must have been defective. Grant Allen (1879), quoted by Parsons (1915), violently criticised this remark. Later Magnus pointed out that the same defect of colour terminology for green and blue, which characterised ancient writings, still exists among many primitive races. But by far the most important contributions on the subject are those of Rivers, as described by Parsons (*loc. cit.*).

According to Rivers, the *Todas*, an aboriginal tribe of the Nilgiri Hills, are colour blind. In early twentieth century, it reached highest frequency recorded in any community. The difference seems to show that even in those *Todas*, there is some deficiency in the sensibility for red. *Todas* are very intelligent and they have small colour fields, probably this is due to definite sensory defect.

The characteristic of all defects of colour vision is that the abnormal people sees fewer hues than the normal. The most common colour blind is the red-green blind.

The colour blindness is broadly classified into two groups (1) total and (2) partial. The total colour blindness is comparatively rare and is due to defective development or complete absence of the cones. The partial form is most commonly discovered in the routine examination while at interview for certain occupations, e.g., railway signal man, motor and engine drivers, sailors, aeronautical services, etc. There are several tests for detecting colour-blindness of which the most reliable and universally adopted procedure is of Ishihara's isochromatic charts.

Colour blindness is an inherited condition being transmitted through a female who is usually unaffected. According to Sorsby (1951), colour blindness has been known to be hereditary since 1778. It is in fact one of the outstanding examples of sex-linkage and it is transmitted as a regular recessive sex-linked character. The general conclusions are: (i) Deuteranopia (green-blind) and protanopia (red-blind) are genetically distinct entities the gene for each being carried by the non-homologous portions of the X-chromosomes (Fig. 1). (ii) The gene determining the deute-

FIG. 1—SHOWING THE HOMOLOGOUS AND NON-HOMOLOGOUS PORTIONS OF THE X-CHROMOSOMES.
b-c = Homologous portion of X-chromosomes.
a-b = Non-homologous portion of X-chromosomes.

ranopia (green-blind) is allelomorphic to that determining deuteranomaly (red-sightedness). Likewise the gene for protanomaly (green-sightedness) is an allelomorph of gene for protanopia (red-blind). (iii) The gene determining normalcy is dominant over the pathogenic allelomorphs and of those the allelomorphs which determine the less severe anomaly are dominant over those for more severe anomaly. (iv) It is likely that the above conclusions may also apply to tritanomaly (blue-defective) and tritanopia (blue-blind). These relations are shown clinically as

Normal > Deuteranomaly > Deuteranopia.
Normal > Protanomaly > Protanopia etc.

The commonest type of transmission of colour blind trait is by recessive sex-linked inheritance with examples of every type of mating. One rare type of transmission is however, reported by Bell and Cunier and quoted by Haldane (1941) in which colour blindness occurred exclusively in females and was transmitted by them to their daughters only and furthermore to all of their daughters. Maternal transmission of this kind, the trait being confined to the females and passed on to the females only cannot be explained on the basis of normal chromosomal behaviour autosomal or sex-linked. Perhaps dysjunction could explain it.

It is difficult to state the percentage of colour blind people in our country because of lack of data. Norman (1934) reported the percentages of colour blind people amongst the railway employees (S. I. Railways). According to him over 10 per cent had some sort of colour defect, 7 per cent were dangerously colour blind and 3 per cent could not distinguish red and green.

Illustrative case notes are appended.

### Case Notes

*Pedigree*—The abbreviated pedigrees are shown in Fig. 2.

The proband, IV-3 attended the R. G. Kar Medical Hospitals with a history of loss of vision in both eyes from his second year of life. He was diagnosed as a case of primary pigmentary degeneration of the retina and was referred to one of us (J.B.) for tissue therapy. While examining his other siblings for the presence of any retinal pathology, it was noticed that one brother and one maternal uncle were suffering from colour-blindness (Ishihara's isochromatic charts). As far as could be detected there was association of myopia with colour-blindness in all the affected members excepting one, viz., the proband, who was not a myope. Except for IV-3, IV-5 and III-13, all members seemed normal. II-7 died of coronary thrombosis in 1942 at the age of 58, III-12 died of pulmonary tuberculosis about one year ago at the age of 41 and that she was not colour blind was proved early in her life by an ophthalmologist, IV-2 died of dysentery at the age of 7 months, IV-6 was stillborn, IV-8 and IV-9 were babies and so the examination was not possible. I-1 was a priest by profession, so it was difficult to surmise whether he was a colour-blind person or not.

II-5 (Mrs. I. B., aged 56) was neither colour-blind nor myopic. The media was clear and fundi oculi normal in both the eyes. Bleeding time was 2 minutes 50 seconds and clotting time was 4 minutes.

II-7 was a civil engineer by profession. He was a good painter and a photographer. Probably he was not colour blind.

III-13 (Mr. B. N. B., aged 38) was an incomplete red-green blind with complete green blindness, which was detected at the age of 9 years and confirmed at the age of 21 years at an interview for air service. He was a

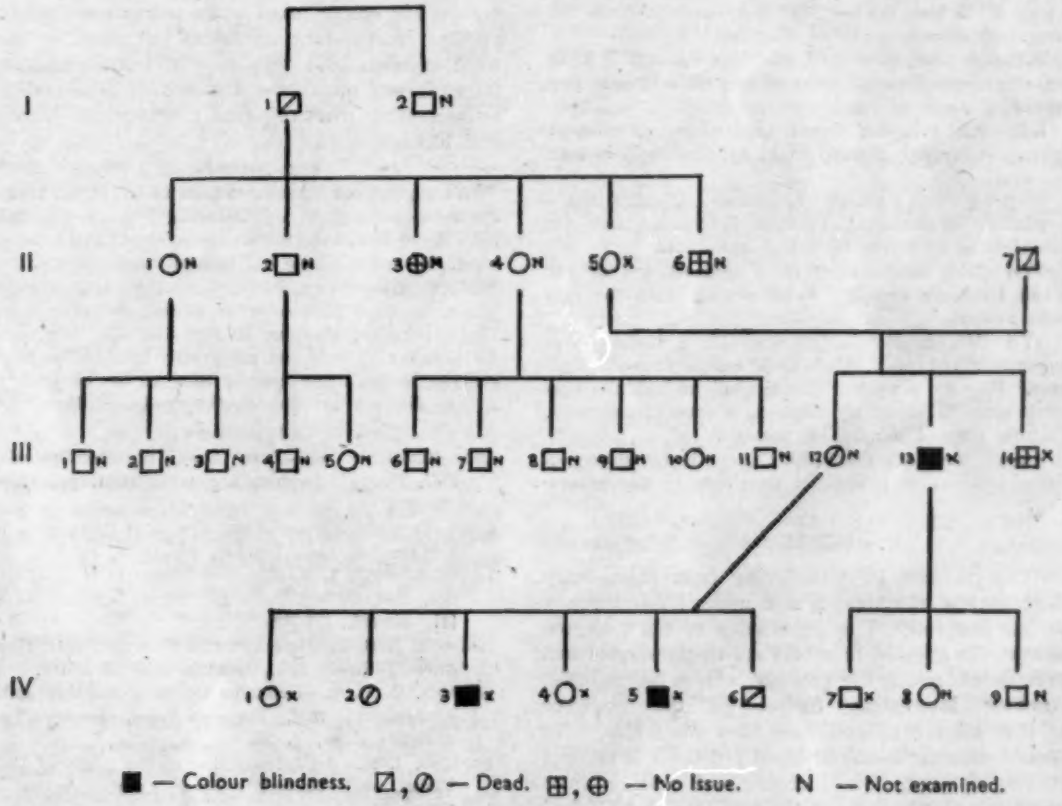


Fig. 2—Pedigree Chart of 'B' Family Showing Sex-Linked Heredity.

myope and he had got a divergent squint in the right eye. Fundi oculi in both the eyes were normal excepting a few choroidal vessels which were seen at the periphery. Bleeding time was 2 minutes 25 seconds and clotting time was 3 minutes 10 seconds.

III-14 (Mr. N. B., aged 36), was neither colour blind nor a myope. Fundi oculi in both the eyes were normal. In the left eye there was a white spot at about 7 o'clock position of the pupillary margin being attached to the posterior surface of the iris at the pupil. It was believed to be congenital in origin and pupillary reaction in that eye was normal with very good maintenance.

IV-1 (Miss L. G., aged 23), a teacher by profession, was myopic but not colour blind. Fundi oculi in both the eyes were normal.

IV-3 (Mr. A. K. G. Sr., aged 21) was the first case which came under observation. This unfortunate young man became blind at the age of 1 year and 4 months. His maternal uncle (III-13) said that after an attack of chickenpox at the age of one year and 4 months he suddenly lost his vision. He was intelligent, sharp in conversation and a very good singer. At the time of investigation he had extensive bilateral pigmentary degeneration of the retina with divergent squint in the left eye. There was also coarse horizontal nystagmus in both the eyes. In both the eyes, the discs were pale and the foveal reflexes could not be identified.

R.E.—No hand movement was there but P.L. P.R. of white light was present. There was no coloured light perception.

L.E.—P.L. P.R. was absent (both white and coloured light). Retinoscopy showed slight hypermetropia in both the eyes.

Bleeding time—3 minutes 30 seconds. Clotting time—4 minutes 40 seconds. Detailed fundoscopy was not possible due to coarse horizontal nystagmus.

IV-4 (Miss S. G., aged 19, a student) was neither colour blind nor myopic. Fundi oculi in both the eyes were normal.

IV-5 (Mr. A. K. G. Jr., aged 17, a student) was incomplete red-green blind with complete green-blindness. He was a myope. Fundi oculi in both the eyes were normal. Bleeding time—2 minutes 20 seconds. Clotting time—4 minutes 40 seconds.

Others were not examined. There is no history of consanguineous or inter-racial marriages in any generation.

## Discussions

The proband IV-3 (suffering from pigmentary degeneration of retina) is now under tissue therapy in our hospital. The peculiarity of the pedigree is that the affected members are deuteranopes and myopes excepting the proband who is not myopic. Another interesting feature of the pedigree is that all the affected members are males. No female member is colour blind but there is myopia in one of them. The bleeding and clotting times were examined in generations II, III and IV and they were found within normal limits. It is difficult to correlate the two conditions with our meagre stock of genetical data but it is interesting that Haldane (1941) quoted a pedigree of myopic blindness and deuteranopia and also reported two pedigrees where there was association of haemophilia with colour-blindness and there also the affected members were males. Recently an interesting pedigree has been reported in which there were sex-linked Duchenne type muscular dystrophy and incomplete red-green colour blindness in one family. Here there is association of myopia with deuteranopia only. But from the table it can be said that II-5 is a heterozygous transmitter. It is difficult for us with our limited genetical knowledge to decide whether females in generation IV are normal or carriers; possibly marriages and their issues will decide the issue.

## Summary

A family of red-green colour blind with sex linked heredity is reported. The proband, a young man of 24 years, had been suffering from blindness due to primary pigmentary degeneration of retina. Some of his male siblings were both myope and colour blind while the females were all exempt from colour blindness but some of them were myopes. No tendency of haemophilia was found in any member of the family. The pedigree is interesting from the aspect of multiple heredity and linkage.

### Acknowledgments

We express our sincerest thanks to Dr. N. K. Munshi, Professor-in-charge of Ophthalmology, R. G. Kar Medical College Hospitals, for kindly referring to us the proband. We acknowledge our grateful thanks to Dr. S. N. Bose, Superintendent, R. G. Kar Medical College Hospitals, for kind permission to publish the case records. Our thanks are also due to Mr. Atul Kr. Bose, artist, for sketches. Lastly, we are greatly indebted to Bhattacharyya brothers who used to come to the hospital from a long distance to establish the sex-linked heredity.

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# INFECTIONS AND GANGRENE OF THE FOOT COMPLICATED BY DIABETES

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Diabetic patients and their tissues are less resistant to traumas and infections. Inflammations and infections otherwise considered trivial have at times far-reaching effects in the diabetics. Infective organisms grow more easily in their tissues. Once settled, infections tend to spread more rapidly and cause more tissue damage. Very often they lead to spreading cellulitis and at times gangrene. The diabetic state is made worse during acute infection.

The reasons for lowered resistance may be generally stated to be due to:

I. *Metabolic changes*:

(a) Decreased activity of blood elements associated with resistance to infections—
  (i) Subnormal activity of phagocytic capacity of leucocytes.
  (ii) Subnormal bacteriostatic and bactericidal action of whole blood.
  (iii) Subnormal activity of the components.
  (iv) Lowered state of general cellular nutrition.

(b) Increased percentage of sugar in the tissues.

II. *Vascular changes*:

As time goes by tissue resistance is lowered due to creeping changes in the local vascular mechanism and the advent of progressively increasing arteriosclerotic changes. The changes take place in the muscular arteries of the foot. They progress undetected as they are not attended with any characteristic clinical phenomena. The pulsation of the posterior tibial at the ankle and the dorsalis pedis may be feeble or absent. In spite of this the collateral circulation may remain satisfactory for a fairly long time in many cases and adequately maintain the nutrition of the limb.

As age advances ischaemic changes commence to manifest themselves. The foot, specially the toes, commence to get shrunken; nails change their colour and become more thickened and deformed; corns and callosities develop on pressure points; cracks and fissures appear specially in the webs of toes.

The local vascular changes when associated with generalised occlusive changes in the vessels of the limb and generalised arteriosclerosis further undermine the circulation.

III. *Diabetic neuropathy*.

Neuritis does not complicate the younger age groups. Neuritic phenomena are met with in elderly individuals and are manifested by sensory disturbances—pain, paraesthesia, loss of reflexes and different degrees of loss of sensitivity of areas of supply of the nerves without any evidence of motor involvement. Microscopic study of nerve trunks show marked thickening of the walls of intraneural vessels and patchy degeneration of nerve trunks. The capillaries are surrounded by a sheath—the basement membrane. This is thickened. Recent observations show that the basic pathology of diabetic neuropathy is vascular and not due to changes in the spinal cord.

These changes interfere with the nutrition of tissues. Local dehydration and anoxia alter their metabolism. The general system is undermined as a result of defect in the storehouse—the liver and the muscles—leading to increased katabolism with increased mobilisation of carbohydrates and fats and a diminished capacity to store owing to lack of insulin.

It need not be stressed that all these factors do not act equally and simultaneously in every case that come for treatment. Much depends upon
(i) The age of the patient.
(ii) His constitutional make up.
(iii) The age of the diabetes.
(iv) Its previous control.
(v) The life the patient leads.
(vi) Care taken at the inception of trauma and such other factors.

Thus every diabetic patient does not react equally to infection. Children are prone to develop ketosis more easily. With care and control the diabetics of to-day can maintain an equilibrium for a long time. In them infective lesions behave almost in the same way as in the non-diabetics. With proper antidiabetic regime and with rest and judicious antibiotic treatment infections may be better controlled. It has to be remembered that even in these cases the diabetic state is temporarily made worse during acute infections. This is more so in the untreated cases. It is well known that in near about 30 to 35 per cent of the cases the presence of diabetes is detected when an inflammatory mischief sets in or when anticipated response is not obtained in the course of treatment or after an operation.

With advancing age tissue resistance progressively deteriorates. Patients who have deve-

loped vascular instability, arteriosclerosis and neuropathy are real surgical problems. This is more so if associated with generalised arteriosclerosis and other organic lesions such as myocardial damage, vascular changes in the liver and kidneys, nephritic states and so on—the penalties of advancing age.

## Nature and Spread of Gangrene and Infections

### A. GANGRENE :

The diabetic gangrene is essentially a form of senile gangrene in which the process is modified by the presence of sugar in the tissues which offers an ideal pabulum for bacterial growth. It is confined to elderly persons and is essentially an arteriosclerotic gangrene. Trauma is most often the initiating factor. It usually starts in the toes or the sole of the foot with a pre-existing source of infection. Essentially a dry gangrene, infection most often sets in converting the dry gangrene into a moist one with spreading cellulitis.

Sometimes apparently spontaneous gangrene sets in in the toes of the patients suffering from neuritic pains and vascular spasms. Patchy areas of bluish discoloration appear on the tip of one toe or more and spread or a whole toe is found affected. The condition may remain uninfected for months and may spread to the foot, though very slowly. A stalemate is thus created.

Lodgement of emboli higher up in the main vessels of the limb, e.g., the bifurcation of the popliteal specially when the collaterals are deficient leads to massive gangrene with severe constitutional symptoms.

### B. INFECTIONS :

Infecting organisms gaining entrance through cracks and fissures, ulcerated corns and wounds—accidental, self inflicted (e.g., cutting and scraping corns, or fiddling with toe nails) or operative—start the mischief. Their line of spread will depend on the site of infection.

Superficial cellulitis on the dorsum of the foot invariably turns into a deep cellulitis very soon. The skin here is thin ; the subcutaneous fat contains little or no fat and the deep fascia is thin and membranous and entheaths the tendons and tendon sheaths. As such the tendons and tendon sheaths are involved in the cellulitic process. The skin shows inflammatory changes. Pus collects under the skin and if unrelieved causes patchy necrosis of skin in areas exposing a sloughy base. In the sole of the foot however the plantar fascia is not destroyed so easily as here the subcutaneous tissue is thick and fibrous septa divide them into loculi.

Superficial infections on the undersurface of the toes tend to remain localised till their tendons are involved. Then they spread to the sole of the foot into the deeper compartment. The phalanges and their joints are affected by extension of infection along the attachment of the tendons.

Infections from the webs of toes start as superficial cellulitis and unless relieved in time spread to the sole of the foot along the flexor tendons under the plantar fascia. Spread along the subcutaneous tissue also progresses with local signs of infection and a diagnosis of subcutaneous cellulitis is arrived at. The serious implication of a coexisting deep cellulitis may be missed.

The deep cellulitis is limited laterally by the abductors of the big and little toes. The thick inelastic plantar aponeurosis holds the spreading infection under it. Left untreated, the cellulitic process extends towards the heel and burrows to the posteromedial aspect along the second layer of muscles—the tendons of the flexor longus hallucis and flexor longus digitorum—to the inner side of the angle and travels up under the deltoid ligament to the deep compartment of the calf.

Inflammatory oedema and tension under the plantar aponeurosis cause further vascular instability and thrombosis leading to gangrene, specially in ischaemic limbs.

The characteristic pathological change in diabetic cellulitis is sloughing and necrosis of the affected tissues. The accumulation of fluid pus is proportionately much less. As the cellulitis is allowed to progress other muscular compartments are involved. The soft tissues progressively get devitalised and necrosed right up to the bone with a covering of skin that does not show the naked eye appearances of gangrene. In other words, a moist gangrene supervenes on an initial cellulitis.

Nature however is not always so unkind. Various degrees of adjustments often take place so that the host may be spared and the local tissues suffer limited assault.

## Management

In the management of these cases the basic requirements are :

1. To determine the diabetic state.
2. To assess the nature and extent of the lesion.
3. To assess the vascularity of the limb.
4. To judge if emergent surgical aid is necessary.
5. To determine the nature of surgical interference necessary for a particular case.

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6. To decide if amputation is necessary—if so, its site.

7. Rehabilitation and ambulation.

The chief objective of treatment is to control the diabetes and infection *pari passu*. Infective processes render diabetes worse leading to hyperglycaemia and ketosis. Early and adequate eradication of the focus of sepsis and drainage of infective collections are the only means to forestall the onset of coma and avoid catastrophe. This has to be aided by liberal use of suitable antibiotics and a sustained effort to control the diabetes by judicious use of plain insulin and a balanced diet. The chief objectives in the treatment of diabetes in a surgical patient are to prevent acidosis on the one hand and hypoglycaemia on the other. Antibiotics however cannot act as satisfactorily in closed infections as in the presence of oedema, vascular occlusion and necrotic tissues, its diffusion in the affected area is meagre.

The urine of every case coming with inflammatory and infective mischief should be carefully examined—

(1) It is quite possible that the patient had no previous knowledge that he was diabetic.
(2) To find out the perentage of sugar and presence of acetone bodies.
(3) If sugar or acetone bodies or both are detected a blood sugar estimation should be asked for to get an idea of the renal threshold.

The customary early morning urine examination may not give the proper information. Examination of urine passed within two hours of the usual meal is best for the purpose.

The patient should be examined as a whole—special attention being paid to his cardiovascular condition, liver function and evidences of kidney disease and presence or absence of hypertension.

In a good number of diabetic patients arteriosclerosis of some degree is present. Blood pressure studies go to show that it bears no relation to hypertension.

The general and local vascular condition requires careful assessment. This has to be done clinically by noting the local changes in the foot and the presence or absence of posterior tibial and dorsalis pedis pulsation. In some cases dorsalis pedis pulse may be present though the posterior tibial pulsation is absent. These together with the age of the patient and the age of diabetes enable the surgeon to make a fair estimate of the vascular state. Mere absence of posterior tibial and dorsalis pedis pulsation is not an absolute index of advanced ichaemia. Oscillometric readings give more rèliable information. Skiagraphy helps to visualise atheromatous changes in the vessels. Arteriography may help but is better avoided during local inflammation. In some border line cases true evaluation of the status of blood supply of the deep layers of muscles of the foot can be done only at operation.

Based on these examinations and investigations, cases may be classified into three broad groups:

I. (a) The age of the diabetes is young, general health is good and diabetes is under control. In them the prognosis is good and with treatment started early their infections are easy to control and cure.
   (*b*) General condition being the same, the diabetes is detected for the first time or the patients have not been careful about the control of their diabetes. Such patients require more careful treatment and attention to ensure good prognosis.
II. The age of the diabetes has progressed. The patients are in reasonably good health. Local arteriosclerotic changes are not evident. Though the pulsation of the main arteries of the foot is absent, oscillometric reading is favourable, indicating that collateral circulation is satisfactory. With proper treatment at the right time they may be piloted to safety.
III. Elderly patients with established ischaemic limbs. In this group the affection usually starts with gangrene of one or more toes and infection and cellulitis are superadded. When associated with occlusive changes of the main vessels of the limb amputation high up is usually necessary. Otherwise the general rules governing group II will help in many cases. Localised amputations of affected toes or of their metatarsals or midtarsal amputations will be necessary.

In spreading infections emergency operations are called for only when the patients come late and where infection has reached beyond the ankle. The patients are toxic and verging on comatose condition. Early amputation will save life in some desperate cases. In them just enough time should be lost to give protection against hyperglycaemia and ketosis. Intravenous injections of glucose and insulin 40 to 60 units and repeated in smaller doses according to requirement should be given and antibiotics should be used liberally before the operation. The treatment has to be sustained during the post-operative period.

Urgent amputations are also necessary when massive gangrene results from an atheromatous plaque or an embolus blocks the main artery.

In most of the cases it is possible to wait for proper treatment of the diabetes and localisation of infection before operation. In the first group of cases, it may be possible to localise the mischief completely and avoid an operation. But generally the infection will require drainage.

In infections starting from the webs an early incision will prevent the spread to the deeper compartment of the sole of the foot ; so also in infective lesions of the toes.

In spreading deep cellulitis of the sole, great care and judgment is necessary to decide upon the opportune time for operation. If the cellulitis is threatening to spread beyond the ankle, a deep incision sufficient to relieve tension should be made in the first instance without disturbing the vascularity of the part. Upward extension may thus be checked and tension under the fascia relieved. More thorough drainage is left out for a subsequent sitting. In other cases conservative treatment is justified till the general and local conditions are favourable. Too much time should not however be wasted. As soon as possible the infected area should be adequately opened up and thoroughly drained. Incisions in the sole should reach the upper limit of extension. Disorganised soft tissues should be removed as far as possible taking care not to injure the bigger blood vessels. In spreading infection in the diabetics there are more sloughs and sheets of purulent tendons and their sheaths than actual collections of liquid pus. These should be removed. No pockets should be left unexplored. Even after this it may not be possible to remove all sloughing tissues. They have to be left out for local treatment.

The gangrenous toes have to be removed. In these cases the phalanges and the metatarsals are necrosed. The metatarsals are better not interfered with at this stage as they do not help in the spread of infection. They may be removed at a later date as becomes necessary. Often it is found that by the time the wounds are granulating the head comes off as a cap and the wound heals up. If the metatarsals are necrosed it is better to disarticulate them from the tarsometatarsal articulation. Otherwise, wounds do not heal completely till a sequestrated piece comes out. This takes a long time and in these cases very often proper sequestrum is not formed.

Dressings after operation should be on usual lines of wound infection. Patients have to be treated according to requirements. Chlorine antiseptics are preferred at the initial stages. In cases where there are adherent sloughs treatment of the wound with solutions of varidase helps considerably for early liquefaction and removal of sloughs. The wound is packed with gauze soaked in varidase solution and changed several times a day. Early liquefaction further helps by allowing increased diffusion of antibiotics into the diseased area with speedy reduction of infection. Local instillation of antibiotics cannot have the desired effect in such wounds as they are unable to act in the presence of necrotic tissues. Antibiotic powder sprinkled or sprayed on the surface of the wound and round about helps by preventing added infection from the surroundings.

### Choice of Anaesthesia

With the introduction of gas and oxygen anaesthesia, the use of intravenous pentothal, cyclopropane and other nontoxic anaesthetics it is possible now-a-days to carry out more thorough debridement of infected tissues and amputations with reasonable safety. Spinal anaesthesia and regional nerve blocking may be taken advantage of in suitable cases.

### Amputations

#### I. Obligatory amputations :

When amputations become necessary for spreading cellulitis and gangrene the site of amputation should be high up at a safe distance from the upper limit of spread. As such definitive amputations at or above the knee are safe and sound in principle. The advances that have been made in the availability of lower leg prosthesis and the success that is possible to be attained in controlling infections with antibiotics have led surgeons to choose mid-leg amputations more and more in recent years whenever circumstances allow. Unfortunately suitable artificial limbs are not easily available in the country as yet and poor patients cannot afford them. In them amputations at the knee or with a short stump of the upper leg will be more desirable.

#### II. Amputation in ischaemic limbs with superadded infection and cellulitis :

(*a*) When arteriosclerotic changes are generalised and the local vascularity poor or when after incision the wound does not show satisfactory attempt at healing or when toxaemia is marked amputation high up is the treatment. The site of amputation has to be determined on the extent of collateral circulation.

(*b*) In all other cases local amputation after control of infection should be the aim of treatment. The infection should be controlled first by methods already detailed. Shaping of the stump

is better done when the wounds are granulating by removing necrotic remnants of metatarsals. This will leave behind a functional weight-bearing foot if a reasonably healthy soft tissue covering is available.

Older age group patients will appreciate such unorthodox local amputations. They shuffle about quite well on anatomical remnants. But in the younger wage-earning groups of patients who have to stand the strain of physical activity, if amputations have to be performed at the tarso-metatarsal articulations or if the soft tissue stump is scarred it will be better to perform a midleg amputation if they are able to secure a well fitting artificial limb.

III. SPONTANEOUS GANGRENE :

In cases of spontaneous gangrene of the toe without infection when the gangrene remains static sympathectomy may help in improving circulation and then a local amputation may solve the problem.

*CASE NOTES*

## UNILATERAL EXOPHTHALMOS

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A normal or standard position of the eyeball is one in which the vertical tangent to the cornea, at its centre, just touches the superior and inferior orbital margins.

In exophthalmos, the eyeball protrudes out of the orbit. It can be unilateral or bilateral.

Causes of unilateral exophthalmos are many and varied. Broadly they may be (1) inflammatory and (2) non-inflammatory.

The non-inflammatory causes include space-occupying lesions in the orbit, foreign body, exophthalmic goitre etc.

The following is a case report of a case of unilateral exophthalmos due to a very extensive mucocele of the frontal sinus.

### CASE REPORT

A woman, aged about 80 years, was admitted into the hospital on 22-5-54 for diarrhoea and dehydration. Proptosis of the left eyeball was detected incidentally during routine examination of the patient. After the diarrhoea was controlled, the case was referred to for investigation of proptosis. The patient could hardly speak anything and was apparently deaf and hence it was difficult to elicit the history in detail.

*On examination* the left eye appeared proptosed downwards and outwards (Fig. 1, *vide* Plate). There was a swelling just below the supraorbital margin, above and medial to the left eyeball. The eyelids were normal, showing no oedema nor other evidences of acute inflammation.

The exophthalmos was non-pulsatile.

The conjunctiva was slightly congested and showed cicatrisation (trachomatous) on the palpebral surface.

The cornea showed diffuse opacity due to keratitis and lagophthalmos. The conjunctival and corneal sensations were normal. The anterior chamber was normal. The pupils were normal, equal on both the sides and reacting normally.

There was cataract in both the eyes. Light perception and projection of light in all directions were present in both the eyes.

Tension in the left eye was 10 mm. and in the right eye 18 mm. of Hg.

Movements of both eyes were normal except for mechanical restriction of movements (upward and inward) of the left eye due to swelling.

The fundus could not be seen because of corneal opacity and cataract.

Auscultation did not reveal any bruit or murmur over the forehead.

Examination of the nose showed deviation of septum to the left without any purulent discharge or evidence of acute infection of paranasal sinuses. There was no tenderness over any of the sinus regions.

*Laboratory investigations*: RBC—3·8 million/c.mm., WBC—9,800/c.mm. with neutrophils 64 per cent, eosinophils 3 per cent, lymphocytes 32 per cent, and monocyte 1 per cent.

Urine was normal.

*X-ray of the orbit and the paranasal sinuses* showed marked extension of the left frontal sinus with deviation of frontal septum to the right side ; it also showed destruction of the lesser wing of the sphenoid (left side),—a picture suggestive of malignant growth in the orbit or of the sphenoid.

*Screening of the chest* showed old calcified spot in left mid-zone ; no evidence of secondaries.

*Biopsy* was taken from the swelling above and medial to the left eye. While taking a biopsy a little brownish jelly like material came out and this along with surrounding tissue was examined. It showed characteristics of an inflammatory process—no evidence of new growth.

The case was referred to the Otolaryngeal Surgeon of the hospital for opinion and it was decided to explore the left frontal sinus.

*Operation*—A radical frontal sinus operation (left side) was done on 9-7-54. The inferior wall of the sinus was found deficient at places. The whole sinus was full of chocolate coloured gelatinous material (similar to the one removed during biopsy). The sinus cavity was explored. An accessory frontal sinus was found to be present in the retro-orbital region, on the outer side of the main sinus cavity. Bone separating this sinus from the orbit was found to have been destroyed but the periosteum of the orbit was intact and appeared healthy. The ethmoidal sinuses were scraped. The jelly like fluid and part of the sinus wall lining were sent for examination. The opening of the frontonasal duct was enlarged and the wound sutured after packing the sinus.

Postoperative recovery was uneventful but proptosis remained the same; only the swelling supramedial to the left eyeball had disappeared. The wound healed normally.

*Operative specimen*—The tissues sent for examination did not show any evidence of malignancy, but suggested the possibility of a mucocele of the frontal sinus.

About a month after the operation, since the proptosis remained the same and also because of the radiological appearance (Fig. 2, *vide* Plate), the possibility of a retro-orbital growth was thought of as being responsible for proptosis. It was therefore decided to explore the orbit.

*Orbitotomy* was performed on 12-8-54 through a modified anterior approach. The original incision of the radical frontal sinus operation was opened and the sinus explored. The bone covering the ethmoidal sinuses, and part of the orbital plate of frontal bone were found projecting into the orbit preventing the regression of the proptosed eyeball. These bony projections were hard and appeared thick; they were removed. There was no evidence of any other growth behind the eyeball. The eyeball immediately fell back into the wide space thus created by removal of the bony projections. The wound was sutured. During the operation, fibres of the levator palpebrae superioris were damaged.

Postoperatively there was no proptosis, but for a few days there was actually enophthalmos. Due to damage to the levator, there was marked ptosis (Fig. 3, *vide* Plate) preventing the voluntary opening of the left eye.

The bony pieces, removed during operation as revealed in the postoperative radiograph (Fig. 4), showed no evidence, microscopically, of any neoplastic process.

## Comments

In this case the proptosis was therefore due to an extensive mucocele of the frontal sinus which extended far back producing destruction of the lesser wing of the sphenoid bone and displacing and curving of the orbital plate of the frontal bone into the orbit. The ethmoidal sinuses were also markedly enlarged and the overlying bone was thickened and protruded into the orbit which was therefore further reduced in size.

This case is interesting in the fact that besides an extensive mucocele, there was also an element of 'sclerosing osteitis' due to chronic inflammation, which probably accounted for the thickening of the bone over the ethmoidal sinuses. Moreover the destruction of the lesser wing of the sphenoid and the proptosis remaining unaffected even after radical frontal sinus operation confused the diagnosis, suggesting the presence of some neoplastic process behind the eyeball.

Deafness and dumbness apparently had nothing to do with proptosis—incidentally the patient did speak when complaining of pain after operation.

This patient has been followed-up for about two years and there has been no recurrence of exophthalmos, nor any growth suggestive of malignancy.

This case shows the amount of destruction that can be produced *silently* by an extension of the mucocele. The patient never complained of headache and proptosis was an incidental finding.

## Summary

A case of proptosis due to mucocele of frontal sinus is described. It shows the wide extension of the mucocele and also shows the bony projections that might, at the same time, be caused by it, due to sclerosing osteitis.

## Acknowledgments

We thank Dr. Bavishi for assisting us in the compilation of the notes. We are grateful to Dr. O. Chandra, Otolaryngologist, for the radical frontal sinus operation and to Dr. H. D. Patel, the Chief of the Ophthalmic Department, for permitting us to publish this paper. We also thank Dr. L. Monteiro, the then Head of the Pathology Department, now Dean, B. Y. L. Nair Charitable Hospital, for his interest in the case and doing histological examination of material sent, and for allowing the use of the hospital case records.

Fig. 1—Paper electrophoretograms of propositus (No. 6), her father (No. 3), mother (No. 9), brother (No. 1), sister (No. 2) and controls (Nos. 4, 5 and 8).

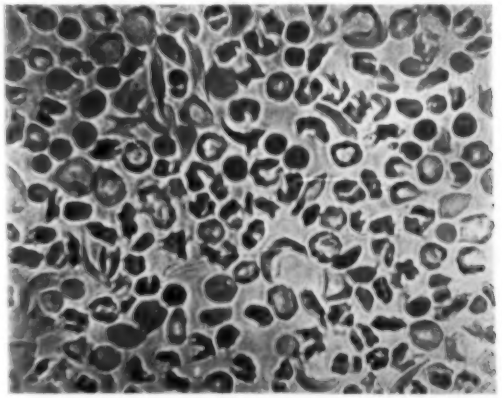


Fig. 2—'Sickling' of patient's peripheral erythrocytes as shown 15 minutes after treatment with 2 per cent sodium metabisulphite solution.

CHATTERJEA ET AL—*Hb. S-Thalassaemia Disease in India ( p. 4 )*

Fig. 1—Showing proptosis of left eye downwards and outwards. Note swelling above and medial to the eyeball on admission.

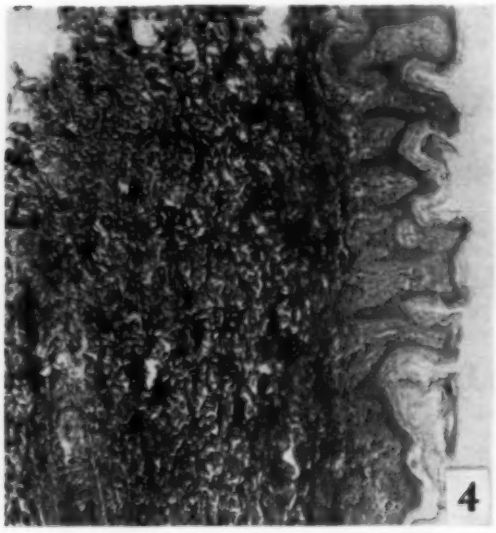
Fig. 2—Radiograph after radical frontal sinus operation, showing the bony projections ( marked + ) preventing regression of proptosis.

Fig. 3—After orbitotomy. Note ptosis due to damage to the levator muscle fibres.

Fig. 4—Radiograph after orbitotomy.

GOKHALE AND DAMANY—*Unilateral Exophthalmos ( p. 19 )*

Fig. 1—Photograph showing hypotrichosis over head and face and absence of pubic hair. Fig. 2—Photograph showing hypoplasia of gums and teeth. Patient had 7 teeth in upper jaw ( 2 central incisors, 2 premolars, 3 molars ) and 6 teeth in lower jaw ( no incisors, 1 canine, 2 premolars and 3 molars ). Fig. 3—Skin from the leg showing hyperkeratosis, absence of pilosebaceous apparatus, sweat glands and excretory ducts. Collagenous bundles are fragmented, pale and hyalinised. H. & E. × 100.



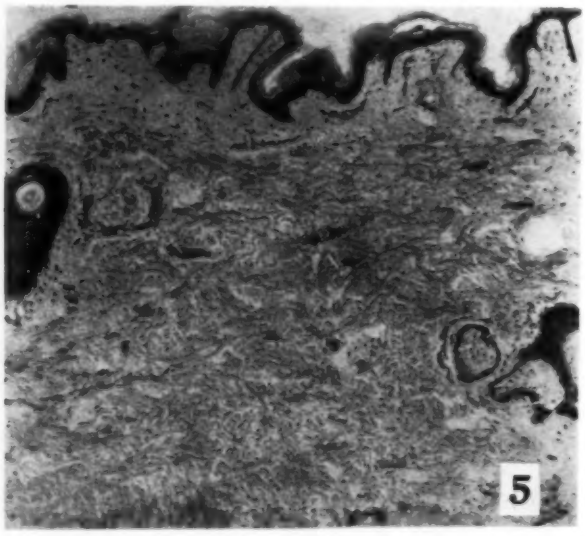


Fig. 4—Skin from the axilla showing conspicuously scanty hair follicles. There are no sweat glands or ducts seen. One of the rudimentary hair follicles from the entire biopsy showing two underdeveloped sebaceous glands. H. & E. × 60. Fig. 5—Elastic fibres are scanty, thinner than normal and fragmented in the sub-epidermal regions, their arrangement is also irregular. Verhoeff's Van Gieson's Elastic stain × 100.



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# CONGENITAL ANHIDROTIC SYNDROME

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Anhidrosis is the inability of the body to produce and/or to deliver sweat on the skin surface.

Congenital anhidrosis is due to developmental defect of the ectoderm. The condition of ectodermal defect was recognised as early as 1838 by Widderburn quoted by Darwin (1892). The term 'Congenital ectodermal defect' was used by Christ (1913), quoted by Goeckerman (1920). Later Weech (1929) after study of some cases of anhidrosis coined the term 'Anhidrotic type of hereditary ectodermal dysplasias' a term which put in a nutshell the aetiology, the pathology and the clinical picture of this syndrome (Cockayne, 1933; Upshaw and Montgomery, 1949).

The main characteristics of this syndrome are anhidrosis, hypotrichosis and hypodontia.

A rare case of congenital ectodermal dysplasia is reported and considered worthwhile from two points of view. That it presents the typical clinical syndrome as given above and also shows an exceptional combination of ectodermal and mesodermal defects.

## CASE REPORT

R. N., 25 year old male, attended the S. M. S. Hospital with complaints of cough with low grade fever, pain in the chest, constipation and pain in the abdomen. There was absence of hair in the outer half of the eyebrow. He was suspected to be a case of pulmonary tuberculosis with endocrine deficiency. Later the patient informed of complete absence of sweating, high body temperature and discomfort during summer.

On further enquiry the patient stated that since childhood he had never observed sweating on his body as others do—even during very hot weather. In summer his body temperature went upto 103-104°F and he kept himself immersed in a water tub or took bath every 1-2 hours. He also felt better when he kept himself wrapped in wet clothes. As far as he remembered none among his relations had this type of disorder.

*On examination*—There was scanty, thin dry hair over the scalp, absence of hair in the outer part of the eye brows and the pubic region (Fig. 1, *vide* Plate), dry rough hair on the face and scanty hair in the axillae. His skin was dry, coarse and thin.

He had hypodontia and maldeveloped gums (Fig. 2, *vide* Plate).

Ear, nose and throat examination revealed atrophic rhinitis, atrophic pharyngitis and external otitis. It is interesting to note that the patient had recurrent attacks of pharyngitis and occasionally epistaxis. There was absence of nasal cilia.

Systemic examination did not reveal anything abnormal except for slight bronchitis at the time of admission.

Blood count, blood chemistry, serology, B.M.R., E.C.G. did not show any abnormality.

*Pilocarpine test*—15 mg. of pilocarpine was injected subcutaneously. This produced marked salivation and vomiting but no sweating could be detected.

*Histopathology of skin*—Two skin biopsies were taken from this case—one from the leg and the other from the axilla. The report is quoted *in extenso*:

Epidermis: The stratum corneum is moderately thickened over the skin of leg and is irregularly forming multiple heavy loose scales of horny substance in the axillary region. The epidermis is thin in both the places about 5 cells thick on leg and 2-3 cells thick in the axilla. The papillae seem to be quite prominent in the axillary region but flattened out in the legskin. No mitotic figures are seen in the stratum germinativum. It is formed by a single layer of darkly stained elongated cells with good amount of melanin pigment. There is plenty of melanin in the basal layer. The rete ridges are irregular in height and conformation in the axilla. Intradermal sweat glands are not in evidence.

Dermal structures: There is irregular distribution of the amount of collagen especially in the papillary region. In the dermis, collagen bundles are thin, atrophic showing fragmentation, hyalinisation (Fig. 3, *vide* Plate), fibrillar disruption but no basophilia. Elastic fibres in the papillae are either absent (Fig. 4, *vide* Plate) or much thinner

than normal when demonstrated by the Verhoeff's and Van Gieson's stain. Elastic fibres in the rest of the dermis seem to be normal. There is mild perivascular lymphocytic infiltration about the capillaries.

Epidermal appendages: The sweat glands, hair follicles, arrector pilorum and smooth muscles fibres are absent from the leg skin but in axilla very scanty and rudimentary hair follicles are seen with occasional sweat glands (Fig. 5, *vide* Plate). A mild lymphocytic infiltration about one of the hair follicles is also present. Sweat glands and sweat ducts both eccrine and apocrine type are conspicuously absent in the two regions.

Diagnosis: Congenital anhidrotic ectodermal dysplasia.

### Comments

This case presents the typical findings of that rare condition of congenital anhidrotic syndrome. Less than 100 cases have been reported in the world literature till 1956. Those with mesodermal involvement have been still rarer (Malagon and Taveras, 1956).

The interesting feature about this case was that the patient sought admission during winter season and presented main symptoms of the upper respiratory tract infection. This on further query was found to be a frequent trouble because of ectodermal defect in the loss of nasal cilia and atrophy of the respiratory epithelium. But as the case was further investigated, he showed all the main features of the syndrome, e.g., anhidrosis, hypotrichosis, hypodontia and repeated rhinitis and pharyngitis. The main complaint of the extreme intolerance to heat was conspicuous by its absence because he was admitted during cold season.

There was little difficulty in diagnosis after the leg skin biopsy revealed agenesis of sebaceous glands, hair follicles, smooth muscles and sweat glands and the axilla skin biopsy showed extremely scanty rudimentary hair follicles and occasional sebaceous glands. The abnormalities of the epidermal appendages were associated with hypoplasia of the collagen and elastica in the upper corium and papillae. The main defects were of ectodermal layer but hypoplasia of the collagen and elastica were suggestive of the involvement of the mesodermal layer too. Altered physiology of the skin was well reflected in the defective skin development and failure to produce any sweating after pilocarpine injection.

Regarding the aetiology the present opinion is that the character may be sex linked, dominant or recessive in different families. In our case no familial or hereditary background could be elicited.

Inspite of this defect there was no sign of intoxication and the renal status and output remained normal. The treatment for the disability is only symptomatic.

There should be rehabilitation of the patient in a cool place.

Treatment of atrophic rhinitis and pharyngitis with oestrogens (Mortimer *et al*, 1937; Herrmann and Sulzberger, 1952) has given good results and is worth trying, taking into account the otherwise longevity of these cases.

### Summary

A case of congenital anhidrotic syndrome with aplasia of gums and hypotrichosis is reported. No familial or hereditary background could be traced here but it was definitely congenital and it showed typical aplastic changes in ectodermal and mesodermal structures.

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## IX MADHYA PRADESH PROVINCIAL MEDICAL CONFERENCE, JABALPUR, 1958.

*The 9th Madhya Pradesh Provincial Medical Conference will be held at Jabalpur on 21—23 February, 1957. There will be a scientific session and an exhibition of medical interest.*

*Details may be had from Dr. R. N. Chatterjee, Organising Secretary, 401, Wright Town, Jabalpur.*

JOURNAL OF THE
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CALCUTTA, JANUARY 1, 1958

## ABNORMAL HAEMOGLOBINS

The knowledge of the existence of two different types of haemoglobin could be traced as early as 1866 when Körber demonstrated the difference between the haemoglobins of the newborn infant and the adult[1]. He showed that foetal haemoglobin was alkali resistant whereas adult haemoglobin could be rapidly denatured by alkali. These two haemoglobins, now known as haemoglobins F and A respectively, are considered to be physiological. Under normal conditions Hb.F is almost completely replaced by Hb.A within the first year of life[2]. Persistence of high level of Hb.F beyond one year of age is a pathological phenomenon seen in hereditary haemolytic anaemias characterised by some form of defect in the normal physiology of haemoglobin synthesis. Though both these haemoglobins are under genetic control, different genes appear to be responsible for their production.

The conception that in addition to two physiological haemoglobins, enumerated above, there may be pathological variants of haemoglobin, is of comparatively recent origin, being first brought out by Pauling and his associates in 1949. The pioneer work of Pauling *et al* demonstrating the difference of electrophoretic mobility of haemoglobin A and that of sickle cell anaemia clearly proved that haemoglobin in the latter condition is an abnormal variant, never found in normal people[3]. This abnormal haemoglobin, later named as haemoglobin S, was found to the extent of approximately 60-90 per cent in sickle cell anaemia and 30-40 per cent in sickle cell trait. Studies in human haemoglobins by various physicochemical methods, particularly by electrophoresis and alkali denaturation technique have led to the recognition of a series of abnormal haemoglobins designated in the order of their discovery as haemoglobins C, D, E, G, H, I, J, K, L. The letter B once assigned to sickle cell haemoglobin was later on replaced by S. Methaemoglobin of Hörlen and Weber[4] awaits recognition as haemoglobin M, while the status of haemoglobin N is still subjudice.

Excepting haemoglobin H on which presently available data are insufficient, all the other haemoglobins seem to be inherited as simple Mendelian characters. Although it is likely that all the variants of haemoglobin A are allelomorphs, direct proof of this assumption has so far been obtained for haemoglobin A, S and C only[5]. Recent studies of Schwartz *et al* show that haemoglobin G is perhaps a normal variant rather than an abnormal type of haemoglobin[6]. Unlike Hb.F, these variants do not differ from Hb.A by their property of alkali resistance or by their visible or ultraviolet spectrum. The so-called M haemoglobin already alluded to is, however, an exception. Haem part of all the other known human haemoglobins is the same, the essential difference being in the constitution of the globin. Some variation in the amino acid composition has also been reported[7-9]. It is quite possible that more critical analysis of these abnormal haemoglobins will bring out fundamental differences in the structure of the polypeptide chains, the number of titrable SH groups, ionisable carboxyl groups and others of more subtle nature[10].

The common mode of inheritance in abnormal haemoglobins is attributed to the presence of specific gene which in heterozygous state does not usually cause any significant handicap to the person concerned[11]. In homozygous state these may, however, produce various grades of haemolytic anaemia. The heterozygous condition is also known as 'trait', the corresponding homozygous condition beieng known as 'disease'[11]. The terms haemoglobinosis and haemoglobinopathy have

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[1] KÖRBER, E.—Inaug. Dissentation, Dorpat (1836). Cited by Bischoff, H., *Ztschr. ges. exper. med.*, **48** : 472, 1926.

[2] SINGER, K., CHERNOFF, A. I. AND SINGER, L.—*Blood*, **6** : 413, 1951.

[3] PAULING, L., ITANO, H. A., SINGER, S. J. AND WELLS, T. C.—*Science*, **100** : 543, 1949.

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[10] LEHMANN, H.—*Acta genet.*, **6** : 413, 1956/57.

[11] NEEL, J. V.—*Medicine*, **26** : 127, 1947.

respectively been proposed for these two conditions[5].

Thalassaemia or Cooley's anaemia represents an inherited defect of haemoglobin synthesis closely related to haemoglobinopathies. In this condition production of haemoglobin A is suppressed while that of F is significantly increased. No abnormal haemoglobin has so far been incriminated as the cause of thalassaemia. The homozygous form of thalassaemia results in severe anaemia whereas heterozygous condition may be asymptomatic or usually productive of milder anaemia. The gene responsible for thalassaemia and that for Hb.A appear to be under independent genetic control. Instances of thalassaemia gene interacting with that of known abnormal haemoglobins—S, C, D, E, G and H, usually manifest as haemolytic anaemias of varying degree.

During recent years there have been comprehensive reviews depicting the geographical distribution, haematological features and various other aspects of thalassaemia and of abnormal haemoglobins[5, 10, 12-15]. Certain parts of Asia and Africa appear to be rich reservoirs of abnormal haemoglobins. Hb.S is found in African Negroes (between the Sahara desert and Zambesi river) and their descendants in other parts of the world, in some Mediterranean races, in Eti-Turks[16], in Veddoids in India and Arabia[10] Hb.C is found mostly in West Africans and in their descendants elsewhere[10, 12, 13]. Hb. D first discovered in a white American family but later on has been reported from Britain, North Africa and in Indians (Punjabis and Gujratis)[10, 13, 14]. Hb.E first reported in a child whose father was in part of Indian origin[17] has since been found in Thailand[13], Burma[10], North Eastern Malaya, Indonesia[20], Assam[21], Bengal[22], Ceylon and recently in an Eti-Turk[19, 23]. Hb.G has so far been reported in two Negro families and one Italian family[10]. Hb.H has been found in Chinese, Philippinos, Thais and one Malaysian of Malaya, in two Greek families, in a Greek and a Transjordanian Arab.[10]. Hb.I first seen in an American Negro has since been reported from Algiers[24]. Hb.J first described in an American Negro family has since been described in West Africa (at first designated Liberia I), in a French Canadian family, in an Indonesian and in a Gujrati Indian[25]. Hb.K has been encountered in Liberia (provisionally named Liberia II) in Kabyles of North Africa and recently in an Indian[23]. Single instance of Hb.L has so far been reported in an Indian[26] (Punjabi Hindu). Thalassaemia once thought to be restricted to Mediterranean races, now appears to be much more widely spread, its incidence in the old world ranging from Western Europe and West Africa in the West to China and Philippines in the East.

*Haemoglobinopathy in India*—Earliest instance of haemoglobinopathy in India was first described in a 2½-year-old Bengali boy from Calcutta[27]. On clinical and haematological evidence, this appeared to be a case of homozygous thalassaemia (Cooley's anaemia), but in the absence of characterisation studies which were unknown at that time, it is not possible to state whether there was any associated abnormal haemoglobin. Since 1938, similar cases have been described from different parts of India, particularly from Bengal, Uttar Pradesh,

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[27] MUKHERJI, M.—*Indian J. Pediat.*, **5** : 1, 1938.

Punjab, Bombay and Nagpur[22, 27-33]. Characterisation studies in these cases have recently shown that many of the so-called thalassaemics represent instances of interaction between thalassaemia gene with haemoglobins E[21] and S[23, 33]. An instance of Hb.S thalassaemia has been recorded elsewhere in this issue[34]. The actual incidence of thalassaemia in different parts of India is not known. In a series of 700 unrelated Bengalee Hindus the incidence of thalassaemia trait is estimated to be 3·7 per cent[35].

The first record of the incidence of sickle cell trait in India was documented by Lehmann and Cutbush[36] in the aboriginal tribes of Nilgiri hills of South India in 1952. In the same year Dunlop and Mozumder[37] reported cases of sickle cell trait and presumptive cases of sickle cell anaemia among the tea garden labourers of Upper Assam originating from the tribal population of Orissa and Bihar. Elsewhere in this issue cases of sickle cell anaemia in a boy aged 4½ years and in his infant sister aged 1 year have been reported[38]. Instances of S haemoglobin have also been recorded amongst the tribal population of Uttar Pradesh[39] and Western India[40] and in Mahars[41] and Kunbis[42] of Madhya Pradesh. A high incidence of 55 per cent has been recorded in Parjah Kondhs[43]. Thus haemoglobin S has been found mostly in the aboriginal tribes.

Haemoglobin E has so far been described in Bengalees and Assamese[21, 22]. Incidence of Hb.E in a series of 700 unrelated Bengalee Hindus was estimated to be approximately 3·9 per cent, an incidence similar to that of heterozygous thalassaemia[35]. The incidence of Hb.E in India thus appears to be lower than that in Burma[19], and Thailand[44] where the incidence approximates 15 per cent and 13·6 per cent respectively.

Haemoglobin D has been recorded to the extent of about 3 per cent in Sikhs from Punjab and 1 per cent in Gujratis[19]. Solitary instance of each of the three other abnormal haemoglobins J, K and L have recently been reported in Indians. No instance of Hb. C, G, H, and I, have so far been encountered in Indians.

Presently available data do not permit any more comprehensive account on the haemoglobinopathies in India. These however, indicate that India is a rich reservoir for abnormal haemoglobins and that haemoglobinopathy, in one form or other, is responsible for mortality and morbidity not only in pediatric but also in general medical practice. Recent advances in therapeutics and public health measures while decreasing the incidence of commoner causes of anaemia, viz., anaemias due to deficiency, malaria, kala-azar and other infections and infestations, are bringing into light increasing numbers of hereditary haemolytic disorders manifesting as instances of refractory anaemias. Extensive survey work in different states and in different communities are obviously indicated to find out the nature and extent of prevalence of abnormal haemoglobins and their impact on population in general. While collecting such data, attention should be given to assess the possibility of the heterozygotes possessing special resistance protecting them against the prevalent infections, infestations and other unfavourable environmental influences to which their normal counterparts are ordinarily more easily susceptible. This study is particularly indicated in view of the contention which now appears fairly well established that in Africans sickle cell heterozygotes are unduly resistant to infection with *Plasmodium falciparum*[45]. In India there is a good scope for evaluating the theory of balanced polymorphism as has been advanced for the perpetuation of genes for abnormal haemoglobins.

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# CURRENT MEDICAL LITERATURE

### Abdominal Pregnancies

ZUSPAN AND OTHERS (*Am. J. Obst. & Gynec.*, **74** : 250, 1957) in reporting on 11 cases of abdominal pregnancy occurring during 1951-1956 observe :

A high index of suspicion resulted in the correct preoperative diagnosis in 8 of the cases. The most common findings were abdominal pain, cessation of foetal motion, vomiting, anterior displacement of the cervix, and unexplained anaemia.

Once the diagnosis was established, immediate laparotomy was the treatment of choice in this series. Adequate blood replacement prior to operation and the availability of at least 4 units of whole blood at the time of surgery are mandatory.

Management of the placenta must be individualised. In this group of patients there was a marked decrease in morbidity if the placenta was removed during the initial operation.

No maternal deaths occurred and only one living child was delivered.

### Vitamin $B_{12}$ and Pregnancy

DUMOUNT (*Presse med.*, **65** :601, 1957, Ref. *J.A.M.A.*, **164** :1621, 1957) writes that vitamin $B_{12}$ can be assayed by biological methods that are difficult and costly and by the more widely employed microbiologic tests. Lactobacillus organisms are used for the microbiologic assay. After reviewing vitamin $B_{12}$ assays on gravid animals, the author describes studies on women during pregnancy, delivery, and lactation, on normal and prematurely born infants, and on women with anaemias that occurred during pregnancy. Vitamin $B_{12}$ deficiency in animals causes disturbances in the reproductive function, such as death of the foetuses, haemorrhagic or degenerative lesions, and malformations. Vitamin $B_{12}$ deficiency in pregnant women generally becomes manifest in the 5th or 6th month of pregnancy. The assay of vitamin $B_{12}$ in the normal newborn infant is generally higher than that in the mother, except when the mother has had a definite vitamin $B_{12}$ deficiency during pregnancy. The placenta is low in vitamin $B_{12}$ content and plays an active role in the transfer of the vitamin only at the end of pregnancy. The prematurely born infant often shows a deficiency of vitamin $B_{12}$, but the administration of this vitamin produces contradictory results in these infants.

Maternal hypovitaminosis is the rule during lactation. The vitamin $B_{12}$ content is elevated in the colostrum and in the milk in the first several weeks of lactation, and then, it decreases, but it can be increased by the oral administration of the vitamin to the mother, particularly in combination with cobalt. Intramuscular injection of vitamin $B_{12}$ in the mother will effect a more prolonged vitamin increase in the milk. Certain forms of megaloblastic anemias in pregnant women can be successfully treated by giving vitamin $B_{12}$, but treatment with folic acid is sometimes more effective. The author recommends the routine administration of vitamin $B_{12}$ to pregnant women, particularly during the last trimester of pregnancy, and to premature infants. The standard prophylaxis and treatment of the anaemias of pregnancy in France consist of the administration of iron, folic acid, and vitamin $B_{12}$.

### Effect of DOCA on the Female Genital Tract

KAISER AND CONRAD (*German M. J.*, **2** :184, 1957) write that injection of desoxycorticosterone acetate (DOCA) in women produces signs of progesterone effect due to the conversion of DOCA into progesterone. Between 10 and 40 per cent of DOCA is converted into progesterone.

The effects of DOCA on genital functions are : (1) production of the secretory phase of the endometrium; (2) development of luteinized cells in the vaginal epithelium; (3) changes in the menstrual cycle in normally menstruating women (early or delayed, occasionally prolonged, anovulatory menstruation). The cycle changes, which occur with preovulatory administration of 20 mg. of DOCA are due to an inhibition of the release of luteinizing hormone from the anterior pituitary gland. No effects on the cycle occur with postovulatory medication. Prolongation of the secretory phase and with it a change in the timing of menstruation only occurs with relatively high doses of DOCA and in combination with the administration of follicle-stimulating hormone; (4) initiation of bleedings in women during monopause or with amenorrhoea; (5) increase in basal and morning (awakening) body temperature. In practice these effects mean that administration of DOCA may lead to abnormal bleedings, especially in the first half of the menstrual cycle and during menopause.

### Lactation and Heredity

WICKES AND CURWEN (*Brit. M. J.*, **2** :381, 1957) from an investigation carried on 943 women (43 per cent primigravida) who were asked at the antenatal clinic about the breast feeding performance of their mothers and from the record of the method of feeding adopted by the women when attending the postnatal clinic observe :

The principal finding was that of 397 women whose mothers were "good" breast-feeders, as defined for the purposes of the comparison, 60 per cent succeeded in maintaining uncomplemented breast-feeding for eight weeks, compared with 43 per cent for the 63 women whose mothers were not "good" breast-feeders.

This association appears to be independent of environmental factors and of the mental attitude of the mothers and their daughters.

In a small series it was shown that the milk yield at the end of the first week is positively correlated with the duration of lactation.

Absolute proof of the influence of heredity is lacking, but the mother-daughter association and the evidence of a twin study (briefly referred to) point to the probability that genetic factors significantly contribute towards lactational failures, 50 per cent of which are otherwise unexplained.

The possible role of heredity and the mechanism of its application in the declining incidence of breast-feeding is discussed.

### Significance of Signs of Foetal Distress

GINSBURG (*Am. J. Obst. & Gynec.*, **74** :264, 1957) from the analysis of a preliminary study of the significance of signs of foetal distress observes :

The signs of foetal distress occurred in 11·2 per cent of 1,363 deliveries. Following these signs the total intrapartum and neonatal mortality was over twice that of the general population.

The most common factors to account for the signs of foetal distress were : cord accidents, labour defects, cephalopelvic disproportion, pitocin spasm, and placental accidents. Age, parity, prematurity, and postmaturity were not important factors in predisposing to foetal distress.

Meconium staining alone in vertex presentations indicates a generally favourable outcome, but it should warn one to be on the alert for the other signs of foetal distress.

Slowing of the foetal heart rate below 100 beats per minute indicates very significant foetal jeopardy. The presence of meconium staining as an additional factor indicates even more severe trouble.

An increased foetal heart rate above 170 beats per minute does not signify severe foetal distress, but the presence of meconium staining as an additional factor may indicate some increase in foetal jeopardy.

Fluctuation of the rate by 40 beats per minute within the limit of 100 to 170 with meconium staining does not appear to indicate foetal distress.

Prompt recognition of the signs of foetal distress and decisive intervention when necessary should prove fruitful in lowering both infant mortality and subsequent evidence of damage to the central nervous system. This is an area of obstetrics in which much can be done by careful intrapartal observation with our present knowledge and facilities until some means is devised by which foetal distress can be promptly and accurately diagnosed.

### Thyroid in Pregnancy

STOFFER AND OTHERS (*Am. J. Obst. & Gynec.*, **74** : 300, 1957) observe :

Anatomic study of 65 autopsy thyroids from pregnant women disclosed that the incidence of goiter is not greater during pregnancy than in the general population.

Actual measurement of the size of follicles and height of epithelium in these 65 glands and comparison with the measurements in 47 thyroids from nonpregnant individuals of the same age revealed that, as a rule, during pregnancy the thyroid has large follicles with abundant colloid and at the same time definite signs of cellular hypertrophy.

Determination of protein-bound iodine and thyroxin in the serum of pregnant women showed a trend toward high values, with PBI values reaching 11·2 μg.

The lack of thyrotoxic symptoms in spite of a higher activity of the thyroid during pregnancy can be explained by a greater demand for, and greater toleration of, thyroid hormone, as demonstrated by a patient with postoperative myxoedema who became pregnant.

### Folinic Acid in Megaloblastic Anaemia of Pregnancy

SCOTT (*Brit. M. J.*, **2** :270, 1957) in reviewing the results of treatment of 19 cases of megaloblastic anaemia of pregnancy and puerperium with folinic acid (leucovorin) observes :

Sixteen received treatment over a limited period till the reticulocyte response reached its peak.

Eleven of these were antenatal anaemias, and though their treatment was discontinued all continued to improve. At term their average haemoglobin was 10·4 g. per 100 ml. and red cell count 3,350,000 per c.mm.

In order to produce a satisfactory response with this short-term therapy, it was found that the folinic acid had to be given in sufficiently large amounts initially (approximately 50 mg.) and that the amount necessary appeared to be independent of the degree of anaemia and the route of administration.

From these findings it seems unlikely that the megaloblastic anaemia of pregnancy is due to an absolute deficiency of folinic acid. Instead the latter would appear to act more as a catalyst at some stage in the haemopoietic process, and evidence is brought forward to show how the demand for folinic acid itself may be further reduced once normal erythropoiesis is established.

### Preclinical Carcinoma of Cervix

LATOUR AND OTHERS (*Am. J. Obst. & Gynec.*, **74** :356, 1957) give in the following lines the summary of their observations :

Extensive cytological examination of the cervix has uncovered a large volume of preclinical cancer.

Theoretical considerations can be based only on universal and adequate ring biopsy or cervical conization procedures and endocervical curettage, together with complete and perpetual follow-up. There are many pitfalls in the solution of this problem, and the difficulties are compounded by conclusions drawn from observations on single or quadrant biopsies, or on conizations without endocervical curettage.

The large number of preclinical cancers detectable by those methods poses new and interesting clinical problems.

There is evidence to support the contention that preclinical cancer should be subdivided into two groups, namely, carcinoma *in situ* and "early invasive," since the latter group does not satisfy the definition of either Stage O or Stage I of the International Classification.

The successful treatment of preclinical cancer of the cervix can be carried out by a variety of methods.

Carcinoma *in situ* can be safely and successfully observed only after the minimal treatment which is incidental to ring biopsy or conization plus endocervical curettage. The conservative attitude is frequently rewarded by subsequent pregnancies.

The dangers of overtreatment appear to be more serious than the theoretical dangers of conservative methods.

Total hysterectomy with removal of the vaginal cuff, and with preservation of the ovaries, appears to be adequate treatment for both carcinoma *in situ* and "early invasive" carcinoma of the cervix.

## CURRENT TOPIC

### TRACHOMA MAJOR SINGLE CAUSE OF BLINDNESS IN INDIA

A three-week National Seminar on Communicable Eye Diseases for paving the ground for a country-wide programme for control of trachoma, was in session (November 11-30) at the Institute of Ophthalmology and Gandhi Eye Hospital, Aligarh.

Ophthalmologists deputed by all the States in India (with the exception of Kerala and Kashmir) and by the Governments of Burma and Thailand attended the Seminar, which was sponsored by the Government of India and the World Health Organization.

Inaugurating the Seminar, Dr. C. G. Pandit, Director of the Indian Council of Medical Research, described trachoma as the "major single cause of blindness in India". He laid stress on the vastness of the problem and the need for evolving techniques and procedures and training of personnel for a mass control programme particularly suited to conditions in India.

#### Varying Incidence

The incidence of trachoma, Dr. Pandit added, varied in different parts of the country and it was particularly high in the States of Uttar Pradesh, Rajputana and Punjab. The Seminar would help in dealing with the disease on a mass scale. The Government of India, he added, were aware of the magnitude of the problem and bearing in mind that modern antibiotic therapy held promise of being an effective means of controlling the disease in its early stages, they advised the Indian Council of Medical Research to consider the steps that should be taken for controlling it. The ICMR convened a meeting of leading ophthalmologists, public health workers and statisticians to review the problem and discuss the ways and means for its control and suggest suitable measures for adoption. It was thus decided to establish a pilot project for the study of the disease, particularly its epidemiology which was so little known, and to work out the principles of a possible mass campaign for dealing with it.

The pilot project in Aligarh was the outcome of this suggestion, said Dr. Pandit. It had been established with the active co-operation of the Government of India and WHO and it was soon realised that for that mass campaign, when initiated, to be effective, it would be necessary to have a large number of trained personnel acquainted with the problem and also with the methods and means of control.

There was much to be learnt about trachoma, Dr. Pandit added, but it was necessary to utilise the existing knowledge for the control of the disease and modify the measures, if necessary, as new knowledge accumulated. The Indian Council of Medical Research realised that there was need to continue the effort in the ensuing years.

#### Planned Approach

Dr. C. Mani, WHO Regional Director for South East Asia, referred to the several facets of the problem of eye diseases and urged a planned approach with due regard for priorities.

Referring to the seriousness of the problem, Dr. Mani gave some striking figures of the incidence of trachoma from parts of India. In a sample survey in the rural areas of Uttar Pradesh, roughly four in every ten of the children under the age of two years were found infected. In the age-group 7-15, eight of ten were infected. Among adults—from 15 years upward—more than eight out of ten were infected. Moreover, among children upto 2 years of age most—86 per cent—were found to be suffering from bacterial conjunctivitis.

Trachoma alone, Dr. Mani pointed out, was not a very contagious disease and it was notable for its tendency to spontaneous cure. In various parts of the world it had disappeared as a public health problem. In India and South East Asia generally it continued to be a major problem because of the prevalence of other eye infections which first vastly increased its chances of transmission, then lessened resistance to the more dangerous diseases and its progress.

#### Living Conditions

These eye infections existed, like trachoma itself, almost entirely because of the conditions under which great numbers of the population lived. That brought to the fore such problems as ignorance of simple hygiene, overcrowding, lack of a safe water supply, proper disposal of human and animal waste and control of flies which played an important part in spreading both trachoma and conjunctivitis. The answer to many of these problems was a programme of health education but it was not just a question of ending ignorance. It involved provision of material improvements requiring considerable capital outlay. Environmental sanitation was the obvious key to the situation. The question, however, was what would be the cost and how long would it be before environmental sanitation in South East Asia made sufficient headway to alter the clinical picture.

Mass treatment alone, as means of prevention and control of trachoma had a limited application, Dr. Mani said. For this reason more attention must be given to control the factors governing transmission. However, for South East Asia this "limited application" was the first feasible and necessary step and this Seminar was directed towards accomplishing it.

He added: "Environmental sanitation and health education find a place in this Seminar and must necessarily do so as long-term, continuing objectives in our field of activities. But our immediate concern is with the immediate need of the people. This is so much the case that the Regional Office for South East Asia is planning to recommend to the Government of India that the initial phase of a mass campaign against communicable eye diseases in India shall begin towards the end of next year".

### Scope of Public Health

Dr. T. R. Tewari, Assistant Director-General, Directorate-General of Health Services, Government of India, addressed the Seminar on public organisation in India and the health trends in the country. It was in keeping with the current concepts of public health, Dr. Tewari said, that a seminar on communicable eye diseases should have as its backdrop a broad view of health conditions in general. Tracing the evolution of health services in India, Dr. Tewari described how their purely curative functions had been enlarged, over the last 100 years, to embrace today's broad-based, planned public health programmes. Public health was increasingly being recognised as an expression of the composite health of many people with a social rather than individual objective, he said. The goal of health services today could not be limited to the care of the sick or provision of hospitals. They had to have a much broader aim which must include, in addition to medical facilities, such measures as control and prevention of communicable diseases, environmental sanitation, safe water supply, food hygiene, care of mother and child, provision of laboratory services, facilities for statistical studies and health education of the public.

### Aims of Seminar

Addressing the participants on the scope and objectives of the Seminar, Dr. M. Radovanovic, Senior WHO Officer at the Trachoma Pilot Project, said the Seminar was primarily aimed at helping young ophthalmologists to gain further experience in the clinical and laboratory diagnosis of trachoma with particular stress on the way in which the infection spread. It was important to remember, he said, that an ophthalmologist, when presented with the patient, looked not merely at an eye, in which he was trained to recognise the presence of the particular disease, but at a human being whose environment, culture, and personal habits had made him vulnerable to trachoma or conjunctivitis and had largely decided their cause and severity.

Study of the methodology of field investigation was the next objective, for field investigation was the means by which could be obtained the essential body of knowledge which must be the basis of all future action.

### Human Approach

"If our approach to the people is one of patience, kindness and, above all, of understanding, we shall get in return not only acquiescence but the actual and essential collaboration which we need if we are to help them. Public health rests on public relations", he said.

The Seminar also aimed at giving the participants more experience in trachoma control, Dr. Radovanovic said. Control methods, he added, could not be learned by rote and be rigidly put into practice in every field; they might be basically similar but must be sufficiently flexible to change according to the line which local conditions suggested.

The participants in the Seminar and the guests included representatives of WHO, UNICEF and ICMR.

## NOTES AND NEWS

### Radiation Protection in X-ray and Radium Therapy

A WHO consultant on hospital physics is on a tour of India with the purpose of giving lectures at centres of radiology, and also advising in his subject as required.

There is a good deal of interest in India at present concerning radiation protection in the diagnostic and therapeutic applications of x-rays and in radium therapy. In the past radiation effects on the body were largely considered as having a threshold below which no effect was produced: in recent years, however, there has been increasing evidence that some radiation effects, e.g., genetic, have no threshold below which harmful effects are completely absent. Many countries are therefore looking into ways by which radiation in excess of that necessary for the success of any particular diagnostic procedure may be eliminated. The same may be said for radiation received by medical staff in radiotherapeutic or other work.

Mr. R. F. Farr, deputy chief hospital physicist at the Christie Hospital and Holt Radium Institute, Manchester, will lecture at various radiological centres in India on the British approach to this problem, and will also give advice, if required, on hospital physics in general. His itinerary includes visits to Lucknow, Madras, Bombay and Calcutta. He is also visiting Ceylon.

### World Medical Periodicals

In October, 1957 the second edition of *World Medical Periodicals* was published by the World Medical Association.

The revision of this volume has been continued during the past two years and as a result, some 1,400 new titles have been added and some 600 omitted. The new edition contains the titles of medical, pharmaceutical, dental and medical veterinary periodicals which were in existence at the beginning of 1957 and also a certain number of well known periodicals which have ceased publication since 1900 but to which reference is frequently made in current medical bibliographies. In addition to the inclusion of new titles the addresses of the 4,785 periodical titles have been included in the new edition. The new appendices give: 1. A list of the principal international abstracting journals and 2. A list of the principal international periodical indexes.

Other new features in the volume include the International Code for the Abbreviation of Titles of Periodicals as issued in 1954, and the making of the index of periodicals by subject more useful by grouping the index numbers by countries.

### Russian Biological Journals

Complete English translations of four of the most significant Russian biological journals, covering important current research, are available from Consultants Bureau, 227 West 17th Street, New York City. The journals are as follows: *Biochemistry*, 6 issues per year, annual subscription $20·00; *Bulletin of Experimental Biology and Medicine*, 12 issues per year, annual

subscription $25·00; *Biochemistry Section of the Proceedings (Doklady) of the Academy of Sciences, USSR*, 6 issues per year, originally published in 36 issues, annual subscription $65·00. Tables of Contents will be mailed free on request.

These four journals-in-translation are by scientists, specialists in their respective fields, equally familiar with Russian and the technical terminology.

### Russian Biochemistry Symposium

A special issue of the Russian journal "Biokhimiya" to which biochemists from 10 countries and Soviet biochemists have contributed 57 papers, is being published in complete English translation by Consultants Bureau, 227 West 17th Street, New York 11. The 438 pages issue commemorates the 100th anniversary of the birth of A. N. Bakh, who is hailed as the father of Russian and Soviet biochemistry. Bakh was the founder of the Soviet journal "Biokhimiya" in 1936, and edited it until his death.

### New I.C.I. Research Laboratories in England

In October, the new Pharmaceutical Laboratory of Imperial Chemical Industries was opened at Alderley Park, Cheshire, U.K., by Lord Waverley, a former Chancellor of the Exchequer.

An interesting feature of the laboratory is an isolated animal house which cost over Rs. 32 lakhs. Here animals are bred free from natural disease, a constant source of trouble in research. Everything that enters or leaves this 3-storey building must pass through a rigid routine of sterilisation, decontamination and insecticidal sprays; all equipment is thoroughly sterilised, and in an air conditioned atmosphere where the air is changed ten times an hour, the animals live separated by an aseptic 'lock' from the outside world.

### Sixth Meeting of Central Council of Health

The Central Council of Health meeting in its sixth session in Bangalore from January 5 to 7, 1958, will consider an agenda of 16 subjects relating to health policy, health administration and promotion of public health. The Union Minister of Health will preside over the session.

Besides reviewing the progress made in the implementation of resolutions passed at its previous sessions, the Council will consider the recommendations of the Dave Committee in the light of the views expressed by the State Government thereon. It will also discuss a report of the progress made in the implementation of its earlier resolution on the levy of Health Cess and the action taken on the question of framing legislation on the basis of a draft Public Health Bill, as recommended by the last meeting.

Among other items listed for consideration by the Council are progress made in the implementation of the National Tuberculosis Scheme, the difficulties experienced by the Governments in that respect and the various means of remedying them; the progress of the National Water Supply and Sanitation Programme, and as part of that programme, which is a satisfactory method for the disposal of human excreta in urban and semi-urban areas where the water carriage system does not exist.

The Council will also consider the proposal for the interchange of officers on a deputation basis between the Centre and the State Governments to fill senior administrative, specialist and research posts in the Central Health Service and in the State Services.

Another subject which will come up for consideration is that of raising the age of retirement of Government servants to 58 in view of increase in the span of life. The Council will also consider the question of relaxing the requirements of staff prescribed for Primary Health Centres in view of the difficulties experienced in getting properly trained personnel for them.

Whether the enactment of a Corneal Grafting Act, on the lines of the Corneal Grafting Act 1952 of the United Kingdom, as recommended by the All-India Ophthalmological Society, which met at Aligarh in February, 1956, should be taken up and if so, whether such legislation should be Central or State, is another subject for consideration. Also listed in the agenda of the Central Council are the measures necessary for prevention of rabies; measures for checking diphtheria and whooping cough among children, and the proposal for the establishment of "Day Hospitals" for treatment of early cases of mental diseases.

### Progress of All-India Institute of Medical Sciences

The first batch of 50 students (41 men and 9 women) was admitted for the M.B.B.S. course of the All-India Institute of Medical Sciences on the results of a competitive examination held in five different Centres in India, namely, Bombay, Calcutta, Madras, Nagpur and Delhi in September 1956. Five seats are reserved for backward classes candidates. These students are receiving training in Anatomy, Embryology, Histology, Physiology and Biochemistry. A second batch of 50 students was also admitted by the middle of August 1957.

The classes are being held in the College of Nursing building which has been temporarily adapted for the purpose. Laboratories for Experimental Physiology, Histology and Biochemistry have been set up and the dissection hall equipped to enable the students to do dissection work.

The Annual Report of the Institute points out that the main features of under-graduate training during the first academic year have been the stress on the practical work done by the students and the emphasis laid on their learning with visual aids such as slides and motion pictures. Adequate equipment has also been procured for teaching Anatomy, Physiology and Biochemistry.

On the post-graduate side, two students are being given training in the Orthopaedic department. They were admitted in April 1956 for a two year course of training.

### Lok Sabha Passes the Nursing Council (Amendment) Bill

The Lok Sabha on 29-11-57 passed the Indian Nursing Council (Amendment) Bill.

The Nursing Council (Amendment) Bill provides among other things the maintenance of an All-India Register of Nurses. It also seeks to expand the Council with a view to giving greater representation to nursing colleges and Members of Parliament.

### 57-Lakh Hospital at Agartala

The Government of India have approved the proposal for construction of a new 250-bed hospital at Kunjaban, Agartala, at a cost of Rs. 57 lakhs.

The construction of the hospital will be started within the current financial year and is expected to be completed within Second Five-Year Plan period. Government of India have indicated that the new hospital should be constructed with a provision to raise the bed-strength up to 500 later on. When the hospital is completed, the indoor hospital of V. M. Hospital situated in Central Agartala will be gradually transferred to the new site.

It may be mentioned here that the Rehabilitation Ministry, Government of India, have also sanctioned Rs. 4 lakhs or construction of a 50-bed hospital. The tuberculosis hospital will form an annexe to the new hospital to be constructed at Kunjaban.

### Hospitals in Telengana

A comprehensive and co-ordinated plan costing Rs. 21·69 lakhs to improve and develop the district and taluka headquarters hospital in the Telengana region has been sanctioned by the Government of Andhra Pradesh. The amount allotted to district headquarters hospitals is Rs. 14·25 lakhs while the taluk hospitals will be apportioned the remaining Rs. 7·35 lakhs.

The medical institutions in the Telengana zone were sadly lacking in adequate accommodation for patients, and without this facility, they could not increase the bed-strengths in the hospitals. The amounts now sanctioned had been distributed on the basis of population of different districts.

The district headquarters hospitals in Adilabad, Karimnagar, Khammam, Mahboobnagar, Medak Nalgonda, Nizamabad and Warangal would get Rs. 1·33, Rs. 2·25, Rs. 1·12, Rs. 2·25, Rs. 1·80, Rs. 2·02, Rs. 1·33 and Rs. 2·15 lakhs, respectively, while the taluk headquarters hospitals would be sanctioned Rs. 0·02, 1·14, 0·56, 1·02, 0·82, 1·01, 0·64 and 0·99 lakhs respectively. The taluk hospitals in Hyderabad district would be given Rs. 0·55 lakhs.

### Raptakos Medical Research Board Fellowships

The Raptakos Medical Research Board Fellowships for the year 1958 have been awarded to the following candidates for research work on subjects mentioned against their respective names :

1. (Miss) Shashi Bala Prasad, Department of Pathology and Bacteriology, King George's Medical College, Lucknow : An experimental study of the regenerative activity of the islet cells of Langerhans. 2. Kshitish Chandra Das, Institute of Post-graduate Medical Education & Research, Calcutta 20 : Studies on the development of bone marrow hypoplasia with special reference to immunologic mechanism. 3. Syed Hasan Majid, Department of Surgery, Patna University, Patna : Physiological changes following thoracotomy in experimental animals and human beings. 4. Anil R. Sheth, Indian Cancer Research Centre, Parel, Bombay 12 : Biochemical and immunochemical studies of semen and cervical mucus.

## CORRESPONDENCE

*The Editor is not responsible for the views expressed by correspondents.*

### Doctors for Rural Areas

SIR,—I have just gone through a correspondence written by Dr. S. P. Srivastav of Ranchi under the heading 'Doctors for Rural Areas' in the columns of your esteemed journal dated the 16th October 1957.

Being a rural practitioner for the last 28 years in this area, I have a bitter experience about rural practice. The first and foremost of all is that a qualified medical practitioner has to compete with the quacks, who are jacks of all trades, practising allopathy, homoeopathy, unani, ayurveda and what not. The remark about the quacks made by the illiterate mass is that such and such a 'huturi' doctor has many years of experience behind him and he is a good 'dhatujnani'. The illiterate mass and often some of the educated men flock to them specially because they give very cheap medicines.

Malaria was almost extinct for the last 3 years but this year there are stray cases. During seasonal epidemic of malaria hundreds of cases were treated by them and when people got tired of their treatment, getting relapses very often, they came to a qualified doctor for treatment.

The next difficulty which a village practitioner has to face is that of conveyance. In the rainy season besides horses there is practically no other conveyance in the large majority of rural areas.

It was at the Centenary Celebration of the then Calcutta Medical School in the year 1930, in which the late Sir Hassan Suhrawardy in his Presidential Address advised young medical practitioners to disperse themselves in villages instead of huddling together in towns. Had he had experience about the difficulties which a village practitioner has to encounter, he would never have spoken as such.

I do not know why West Bengal Government is not coming forward to give effect to Bhore Committee Report, as the number of qualified practitioners in West Bengal is said to have exceeded the figure stipulated in the Bhore Committee Report. When I started my practice in the year 1930, there were only 5 qualified medical practitioners in an area 6 miles around. The number has increased to about 25 now.

I am etc.

Mangalkot,
Burdwan.

M. A. TORAB.

## REVIEWS

**Combined Textbook of Obstetrics and Gynaecology, for students and practitioners**—Edited by Dugald Baird, B.SC., M.D., D.P.H., F.R.C.O.G. Sixth edition, 1957; E. & S. Livingstone Ltd., Edinburgh and London, Board-bound, 10"×7½", 936 pages with 492 illustrations, 27 in colour. Price 95*s*. net. regd. postage 3*s*.

This well-known textbook appears in this new edition after seven years. This long interval has necessitated extensive revisions throughout the text which fact has naturally made this volume all the more useful to the student or the busy practitioner. Of the original four authors of the first edition (1923) of the book, only one, Prof. James Young, is still a contributor to this edition, while Prof. J. M. Munro Kerr has ceased to be so and the other two are no longer alive. Seventeen contributors have collaborated to produce the present revised and well-edited edition. The well-deserved reputation it had earned, amongst students in particular, is expected to continue and increase with this volume. Besides the first part, dealing with anatomical considerations in two chapters, the obstetric section contains 38 well arranged chapters, in three parts. The gynaecological section contains 14 chapters in two sections. The undergraduate student would find his requirements met with full satisfaction.

**A Student's Histology**—By H. S. D. Garven, B.SC., M.D., F.R.S.E., F.R.F.P.S.G. Board bound 9"×6", 650 pages. E. S. Livingstone Ltd., Edinburgh and London, 1957. Price 55*s*. net, regd. postage 2*s*.

This is an excellent text book and guide for the study of histology, and specially suited for students and beginners in histology. The chapters gradually unfold the knowledge and mysteries of the studies of human tissues, as seen through the microscope by various methods of staining and through the usual magnifications used in the laboratory for teaching human physiology and pathology to students. References to original work have not been included in the text; they have been deliberately omitted. This would specially benefit the beginner who may concentrate on one book only, rather than fritter away his valuable limited time in looking up various references and bigger books. Primarily meant for beginners and students preparing for examinations, the author is naturally more concerned to give to his student reader a point of view, rather than a detailed compendium of facts. The paper, printing, typography, general get-up and size of the book are very commendable to its reader—the student.

**Public Health—The Journal of the Society of Medical Officers of Health**; Vol. 71, No. 2, May 1957. Bailliere, Tindall & Cox., 7 & 8, Henrietta Street, London, W.C. 2. Published monthly, annual subscription 42*s*.

A notification informs all concerned that, with effect from May 1957, Messrs. Baillière, Tindall & Cox. Ltd. have taken over the publication of this periodical, the official journal of the Society of Medical Officers of Health. The opportunity has been taken also to redesign the journal in the present modern manner. Without trying specially to mention any individual article, it gives one satisfaction to find that the six articles published in this issue are interesting, illuminating and useful to public health workers in general, and the members of the Society which this journal serves, in particular.

## OBITUARIES

### Dr. Umasankar Chatterjee

Dr. Umasankar Chatterjee, son of late Nirode Chandra Chatterjee, a renowned physician of Jamalpur, Burdwan, was born in October 1913.

DR. UMASANKAR CHATTERJEE

Dr. Umasankar passed the L.M.F. examination from the Campbell Medical School in 1946 and started practice at Jamalpur. Although a good sportsman in his student life, Dr. Chatterjee did not enjoy good health during his career as a practitioner. He suffered from diabetes for many years and was lately attacked with pulmonary tuberculosis. He died following a bout of haemoptysis on the 5th July, 1957.

Dr. Chatterjee was a popular and an enthusiastic member of the Indian Medical Association, Tarakeswar Branch.

### Dr. R. N. Kackar

Dr. R. N. Kackar was born in the year 1901 in Lucknow. He graduated from King George's Medical College, in the year 1927. He proceeded to England for special training in ear, nose, throat and obtained D.L.O. (London) and Z.L.O. (Vienna). He held the post of Honorary E.N.T. Surgeon to the King George's Medical College, Lucknow, from 1929 to 1934. He was a lecturer in E.N.T. from 1952 to 1953 in the King George's Medical College. He was also E.N.T. Surgeon to the Balrampur Hospital from 1952 to the day he passed away on 4th September 1957.

DR. R. N. KACKAR

Dr. Kacker was popular and a very active worker of the Association and had the unique honour of being elected twice as the President of Indian Medical Association, Lucknow Branch. In his death, Lucknow Branch has lost a stalwart and a great well-wisher of the Association.

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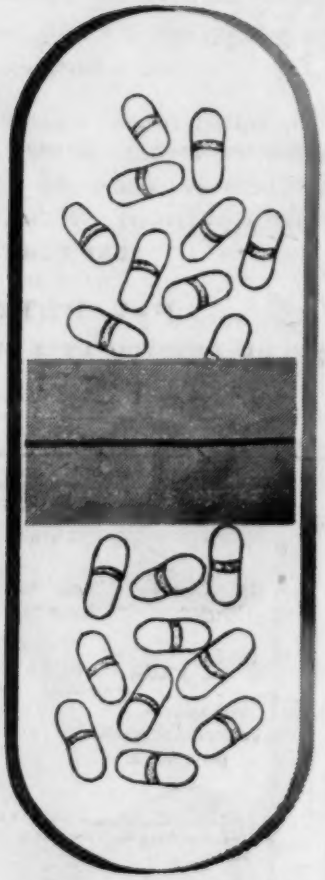

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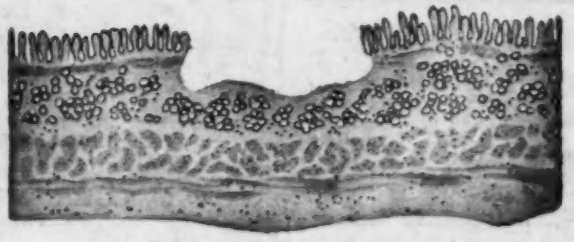

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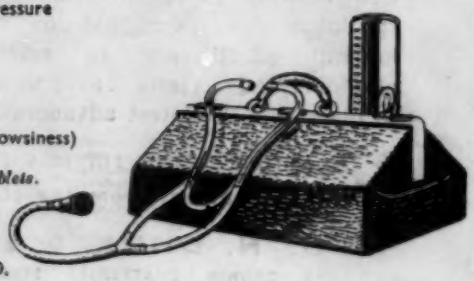

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